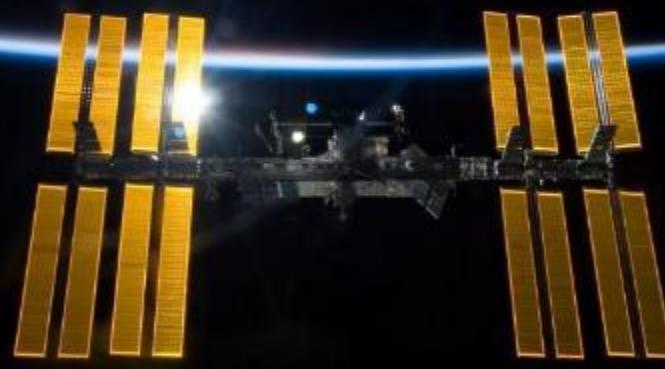




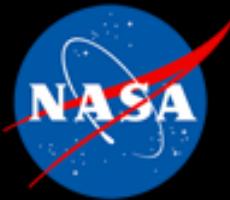
# Long-Duration Space Flight and the Microgravity Ocular Syndrome (MOS)

Tyson Brunstetter, OD, MBA, PhD, FAAO, FAsMA  
Captain, Medical Service Corps, U.S. Navy

Navy Aerospace/Research Optometrist  
Space and Occupational Medicine Branch (SD3)  
NASA Johnson Space Center



Armed Forces Optometric Society Meeting  
Atlanta, GA – 27 February 2017



# DoD Disclaimer

*The views expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U.S. Government.*

*CAPT Brunstetter has no financial interests in any technology or devices mentioned in this presentation.*



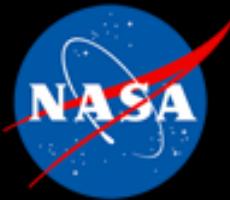


# Acknowledgements

- William J. Tarver, MD, MPH<sup>1</sup>
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- Sara Mason<sup>3</sup>
- Russell Derrick<sup>3</sup>
- Simon Clemett, PhD<sup>4</sup>
- Mayra Nelman<sup>3</sup>
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- Michael Stenger, PhD<sup>1</sup>
- Steven Laurie, PhD<sup>3</sup>
- Brandon R. Macias<sup>3</sup>



1. NASA Johnson Space Center  
Houston, TX
2. Coastal Eye Associates  
Webster, TX
3. KBRWyle  
Houston, TX
4. Jacobs Technology, Inc.  
Houston, TX
5. Universities Space Research Association  
Houston, TX



# Why We Do What We Do...





# Recent Headlines:

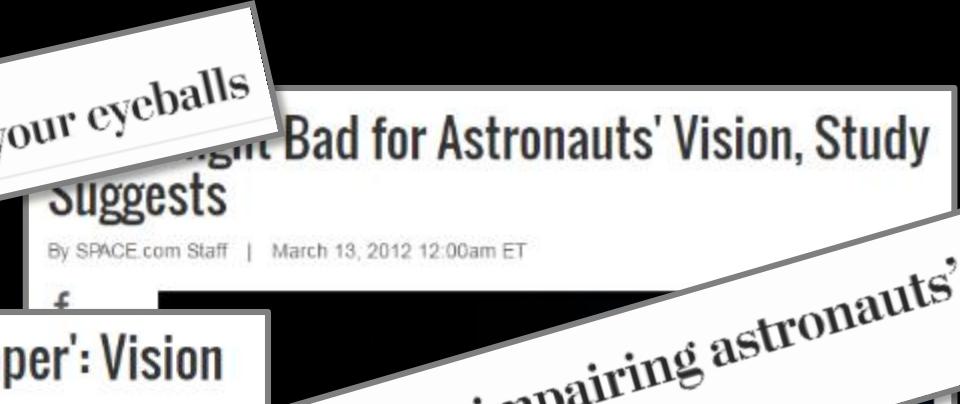
Speaking of Science

## Too much space travel is hazardous for your eyeballs

Bad for Astronauts' Vision, Study Suggests

By SPACE.com Staff | March 13, 2012 12:00am ET

f



## Possible Mars Mission 'Showstopper': Vision Risks for Astronauts

By Mike Wall, Senior Writer | April 8, 2014 07:00am ET

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Health & Science

The mysterious syndrome impairing astronauts' sight

## Astronauts' eyes are at risk after too much time in space

## Astronauts Returning to Earth With Vision Problems

The Washington Post

Astr...  
e vision

Video Channels

POST ORIGINALS | July 25, 2016

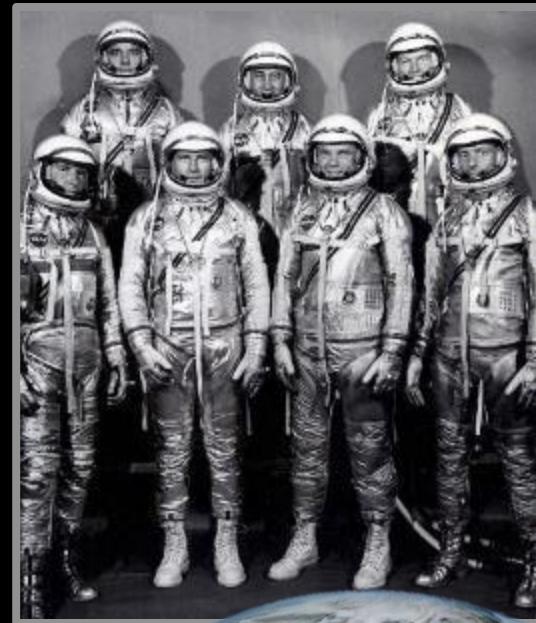
A mission to Mars is causing visual impairment for some astronauts. Will this prevent travel to Mars?

Credit: ESA



# Background: *The Space Environment*

- Bottom-line: Not human friendly. For example...
  - Vacuum: No atmosphere; no air
  - Gravity
    - Holds Earth in orbit w/ sun, and moon in orbit around Earth
    - Gravity reduces w/ distance. ISS (@ ~200-250 mi) feels 90% of Earth's gravity...But...
    - ISS moves at ~17,500 mph, in constant freefall = "Microgravity"
  - Temperature extremes
  - Ionizing (high energy) radiation: Galactic cosmic rays, solar proton events
  - Orbiting space junk/debris: >550K larger than 1cm

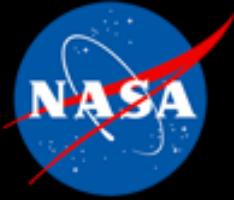




# Background: *U.S. Space Flight*

- “We choose to go to the moon...”
  - **Mercury**
    - $n = 6$
    - Duration: 15m to 1.5d





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\* Person flights; may include multiple-time flyers w/in program



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    - $*n = 33$
    - Duration: 6d to 12.5d



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# Background: *U.S. Space Flight*

## ▪ **Skylab**

- $n = 9$
- Duration: 28 to 84d

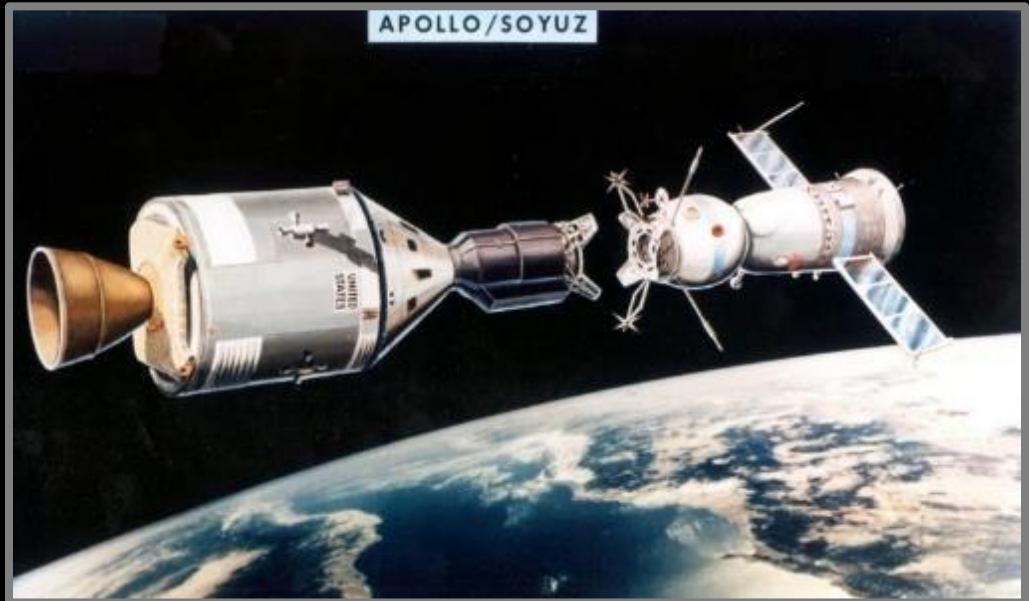


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  - $n = 9$
  - Duration: 28 to 84d
- **Apollo-Soyuz**
  - $n = 3$
  - Duration: 9d



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- **Space Shuttle**
  - $*n = 710$
  - Duration: ~2wk



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  - $n = 3$
  - Duration: 9d
- **Space Shuttle**
  - $*n = 710$
  - Duration: ~2wk
- **Shuttle-Mir**
  - $n = 7$
  - Duration: ~0.5yr



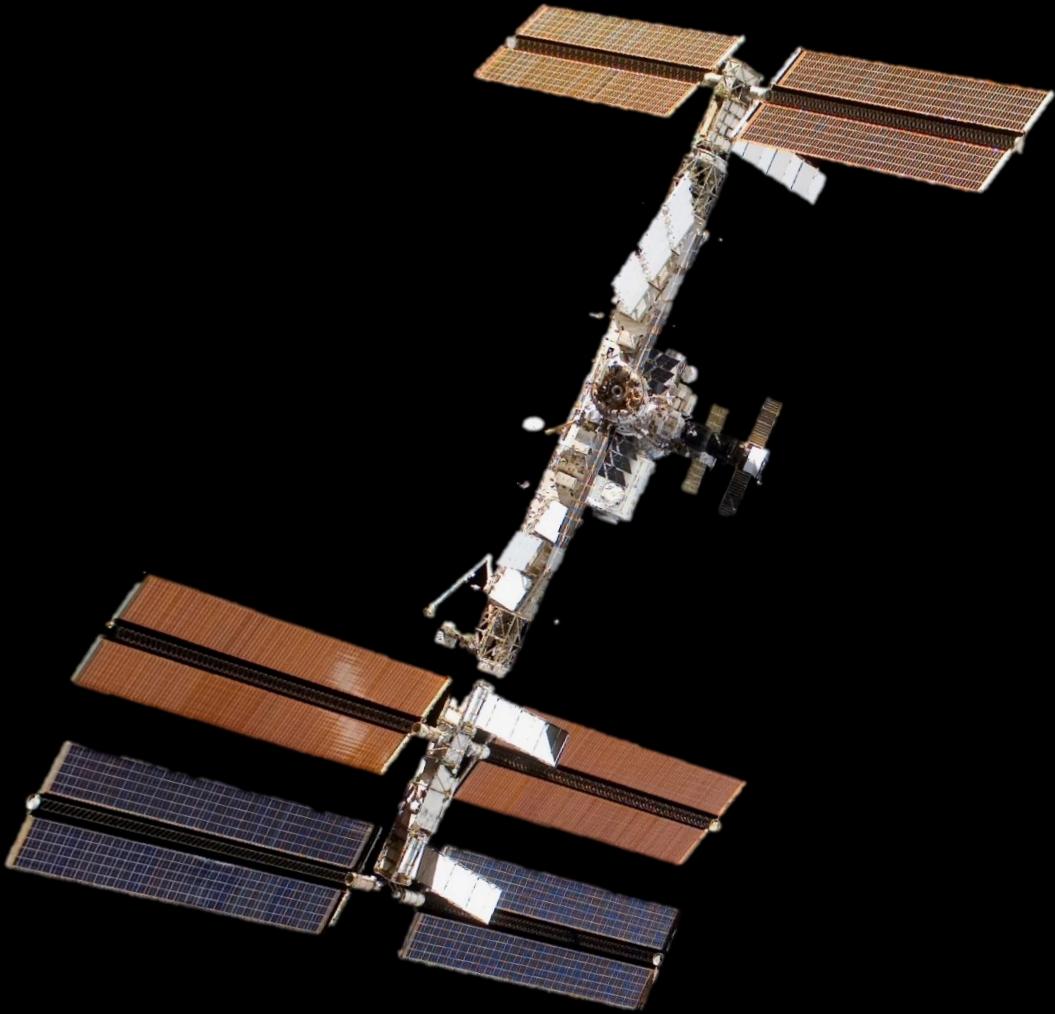
\* Person flights; may include multiple-time flyers w/in program



# Background: *U.S. Space Flight*

## ▪ International Space Station

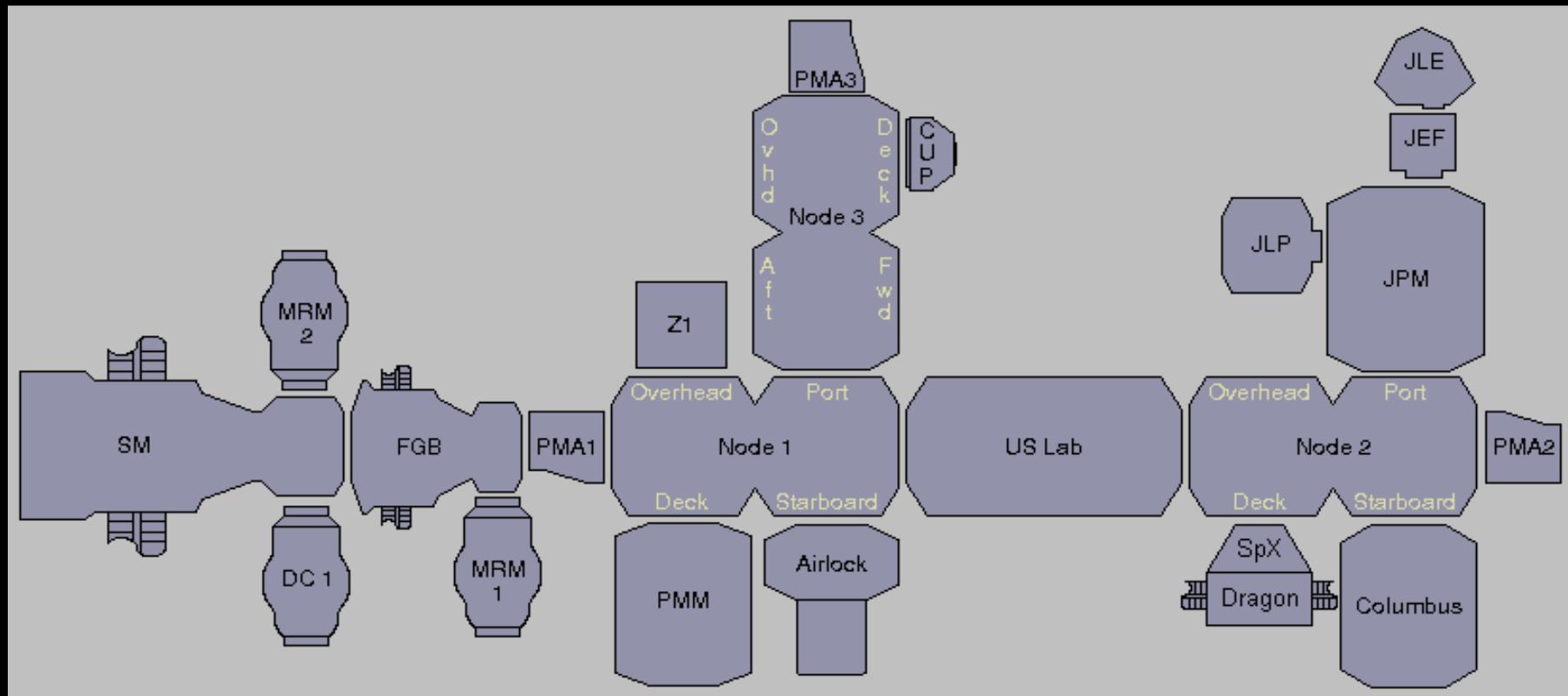
- In use since 2000
- \*n = 58 (as of 31Jan17)
- Duration: ~0.5 to 1y
- International partners
  - United States
  - Russia
  - European Union
  - Canada
  - Japan
- Crew: Typically 5-6
- “Low Earth orbit”





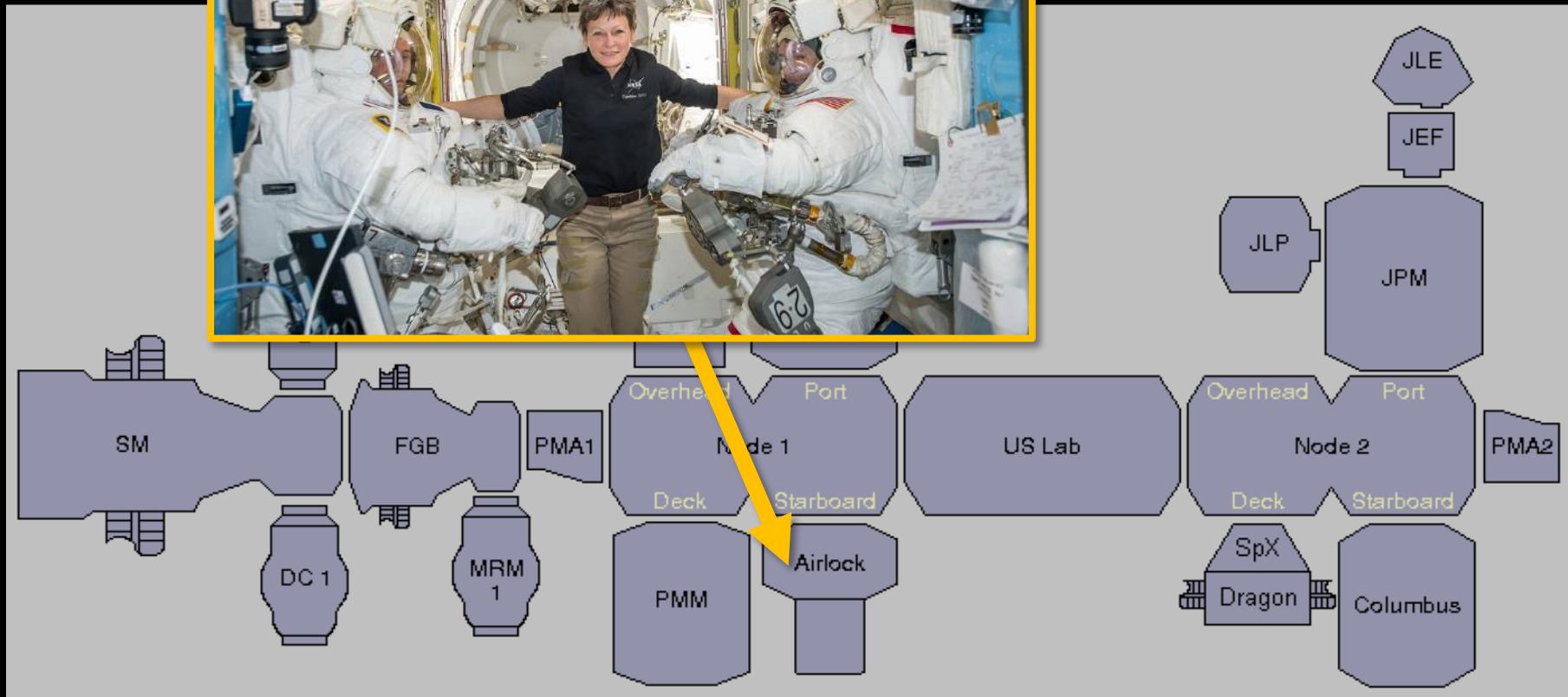
# Background: *U.S. Space Flight*

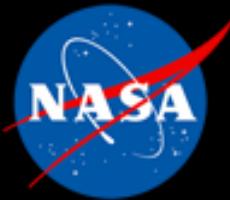
- International Space Station



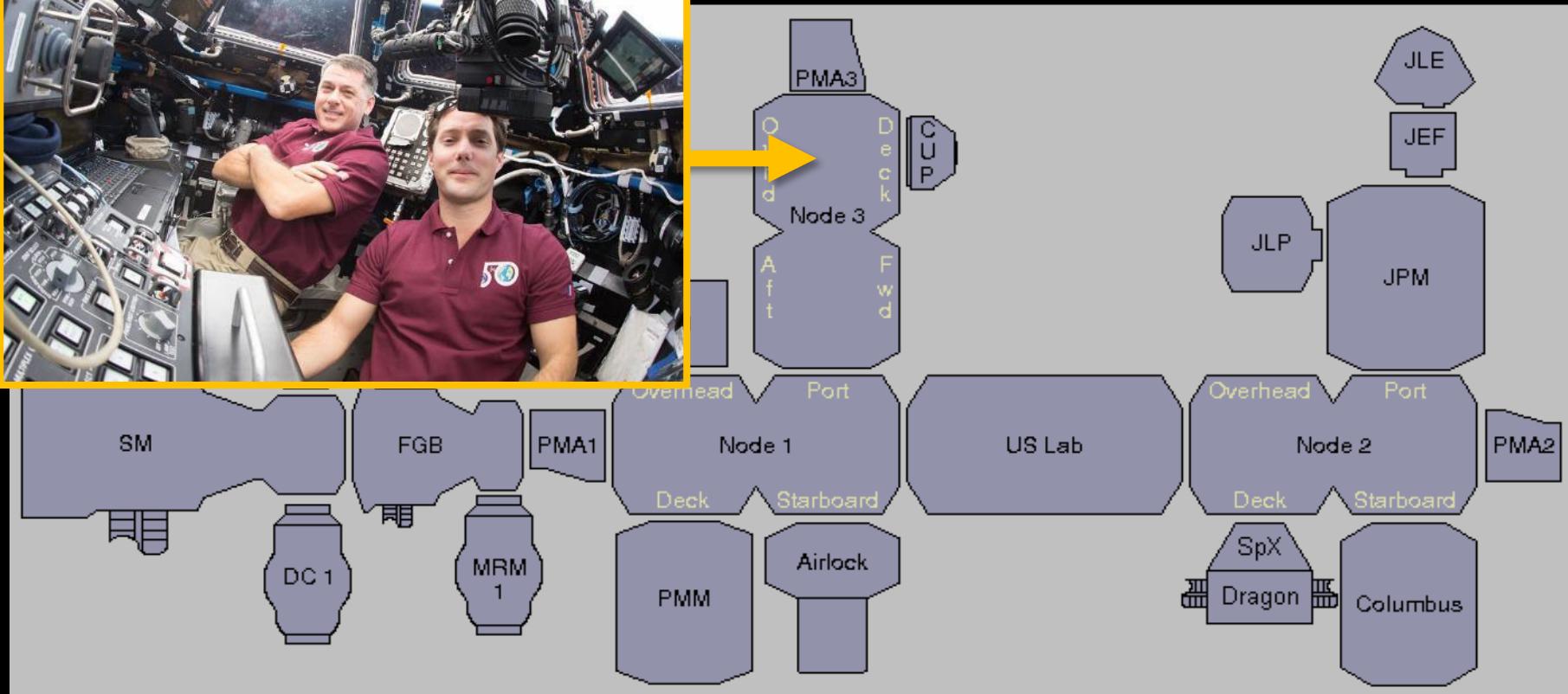


# Background: *U.S. Space Flight*



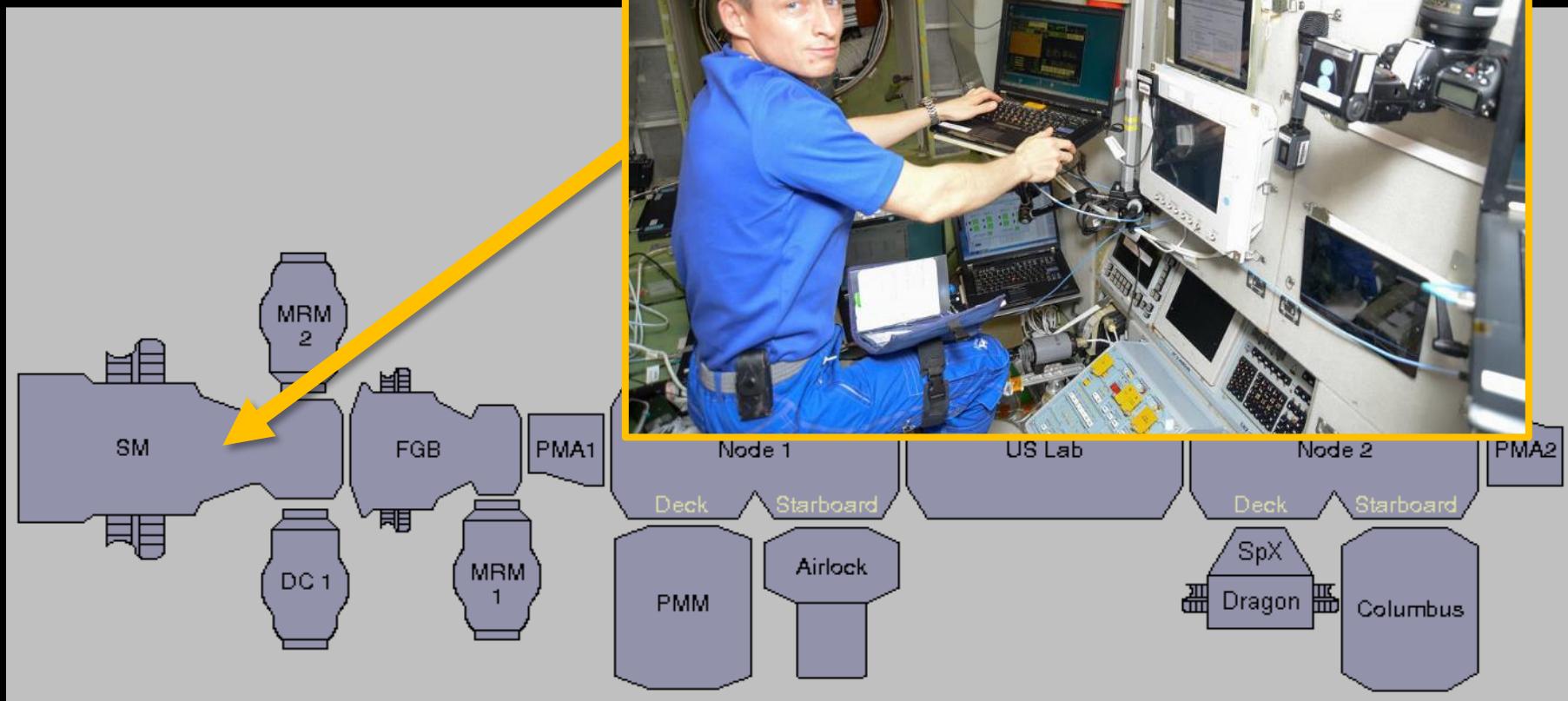


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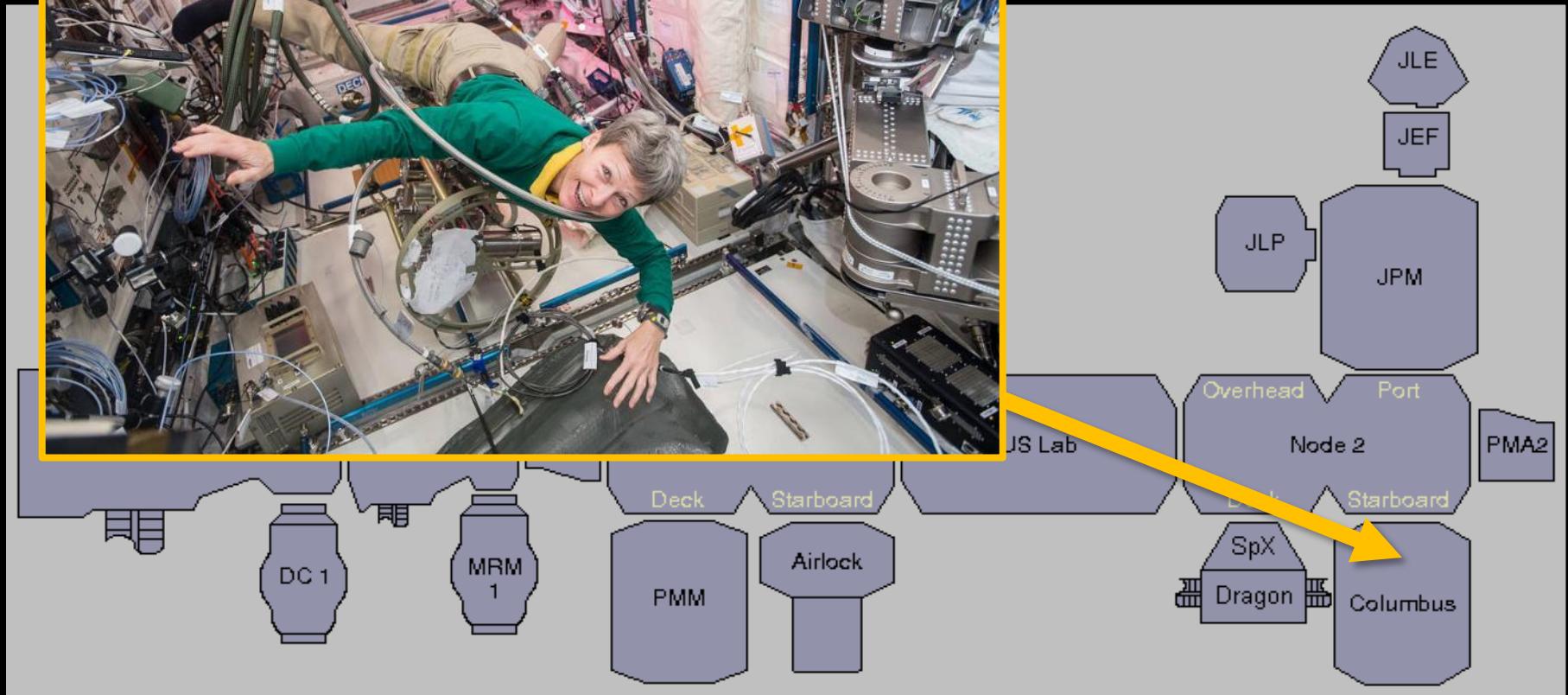


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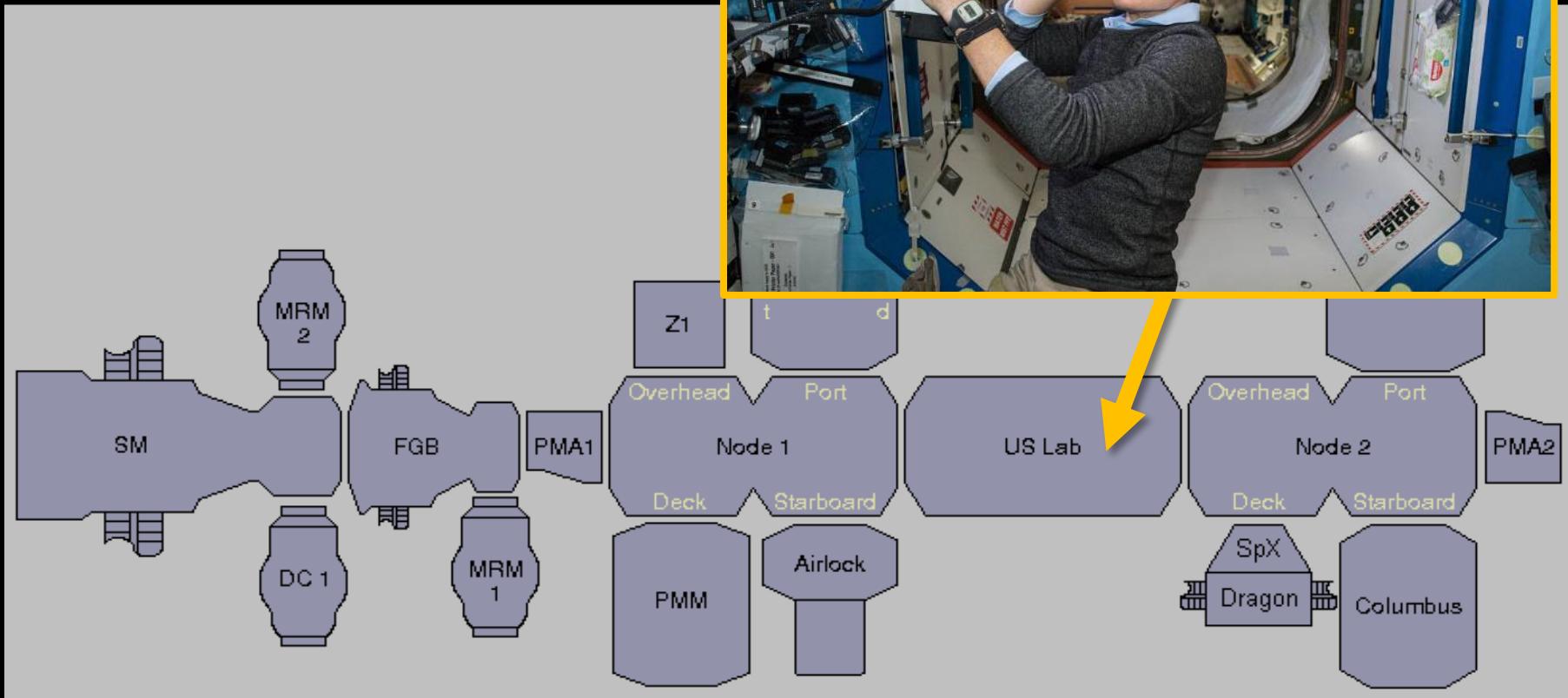


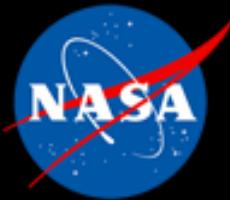
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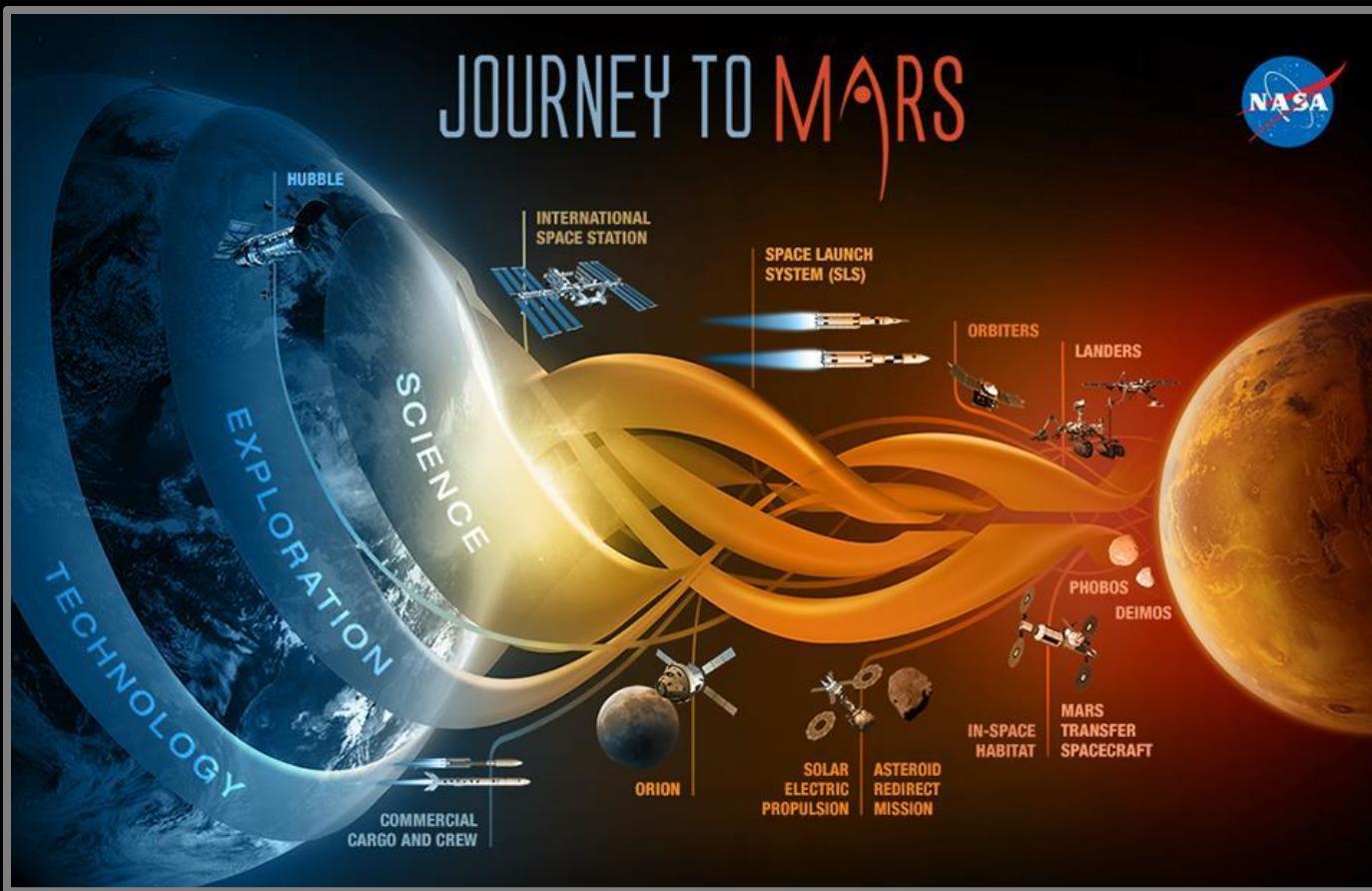


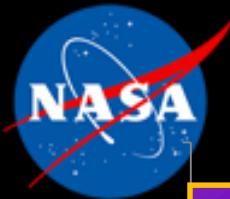


# Background: *U.S. Space Flight*

## ■ The Future...

- NASA to send humans to: An asteroid by 2025; Mars in the 2030s



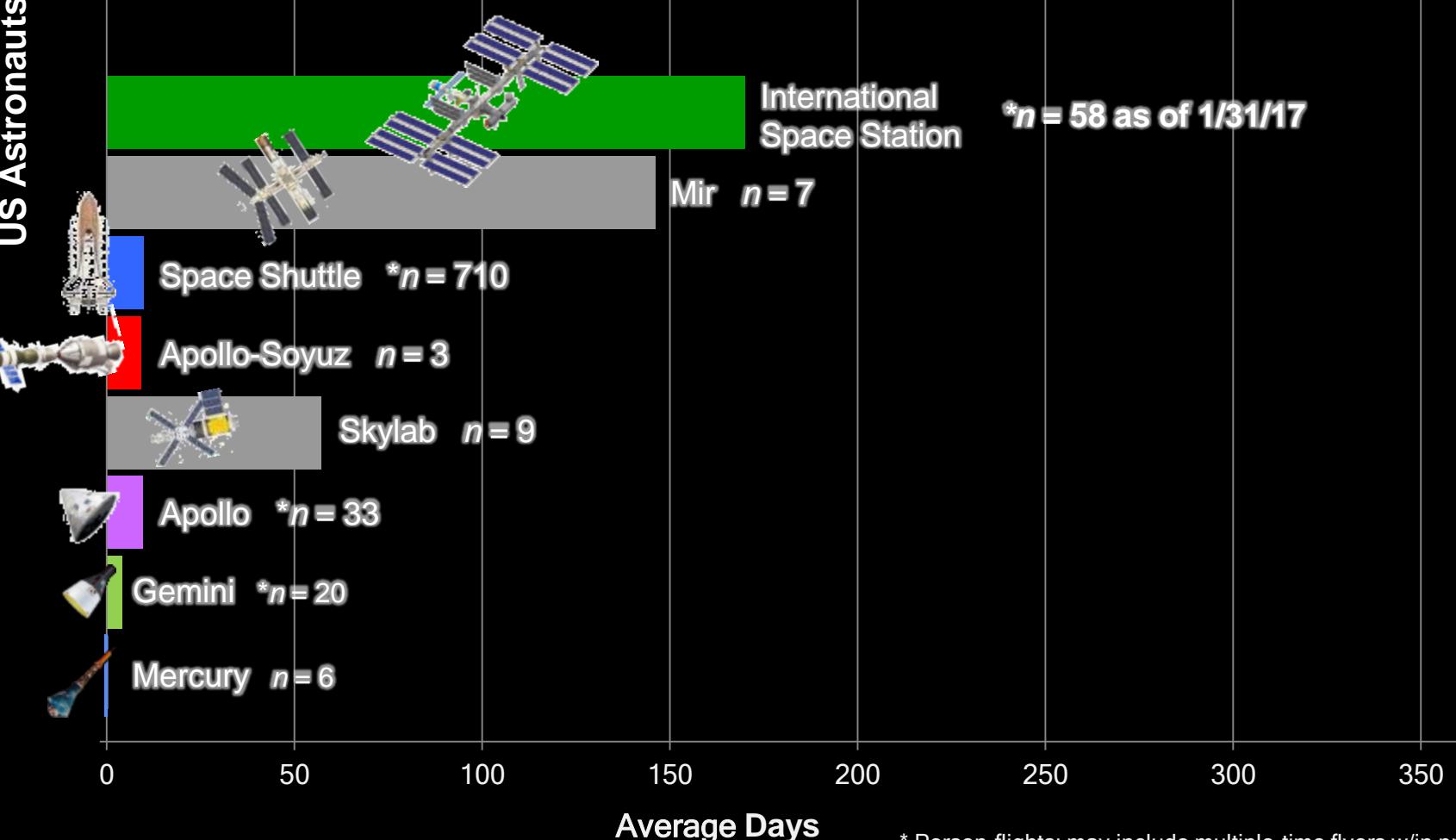


We are just entering, relatively speaking, the long-duration phase of space exposure...

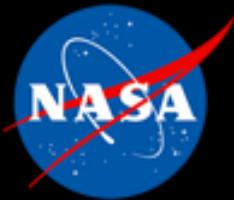
## *Next Generation Missions*



US Astronauts



\* Person-flights; may include multiple-time flyers w/in program



# Background: *Physiological Challenges*

- **Physiological challenges** to astronauts are *substantial*, especially outside of Low Earth Orbit. For example...
- **Muscle Density & Function**
  - Impacted w/in days in space
  - During 2-wk Shuttle missions: reduction in fiber mass
  - Long-term space flight could result in ~40% loss in overall muscular function
    - Increased risk of injury
    - Impeded ability to operate spacecraft & equipment



Bone



Sensory Motor



Cardiovascular



Radiation



Muscle



Exercise



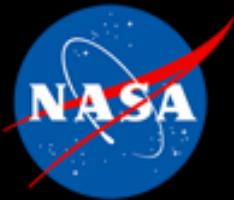
Sleep Cycle



Food & Nutrition



Medical Care

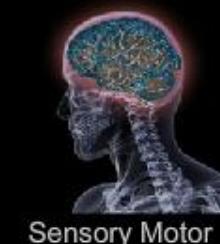


# Background: *Physiological Challenges*

- Physiological challenges to astronauts are *substantial*, especially outside of Low Earth Orbit. For example...
- Muscle Density & Function
- Bone Health
  - In space, bone density lost at ~24x the avg rate on Earth
  - Can lead to kidney stones, fractures, hip/spine problems, impaired healing



Bone



Sensory Motor



Muscle



Cardiovascular



Radiation



Exercise



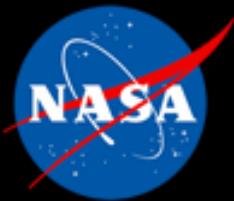
Sleep Cycle



Food & Nutrition

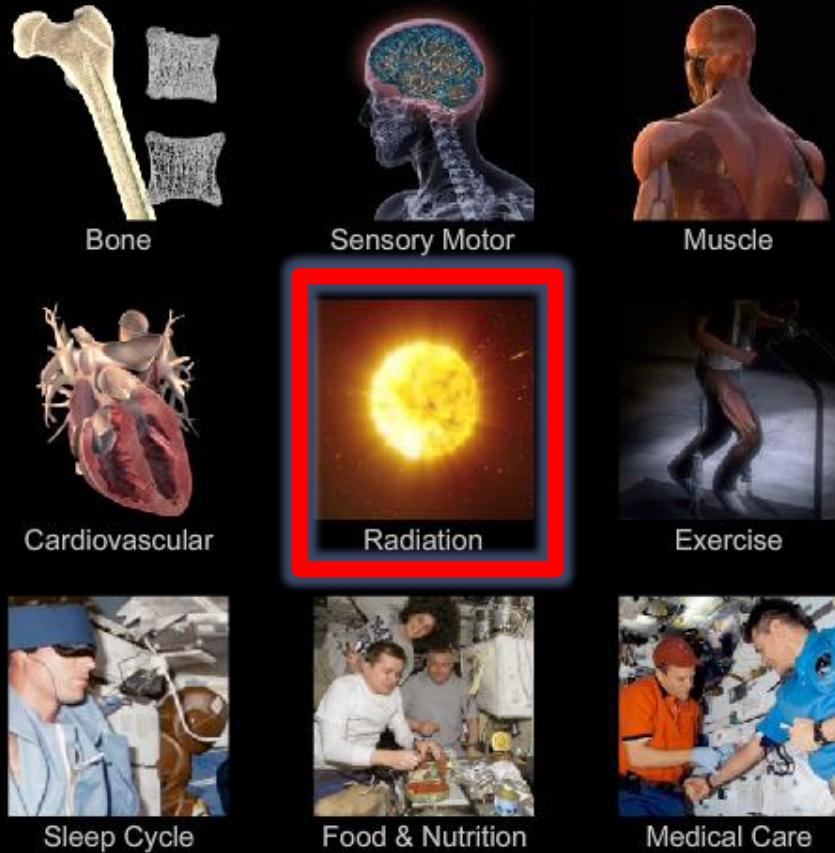


Medical Care



# Background: *Physiological Challenges*

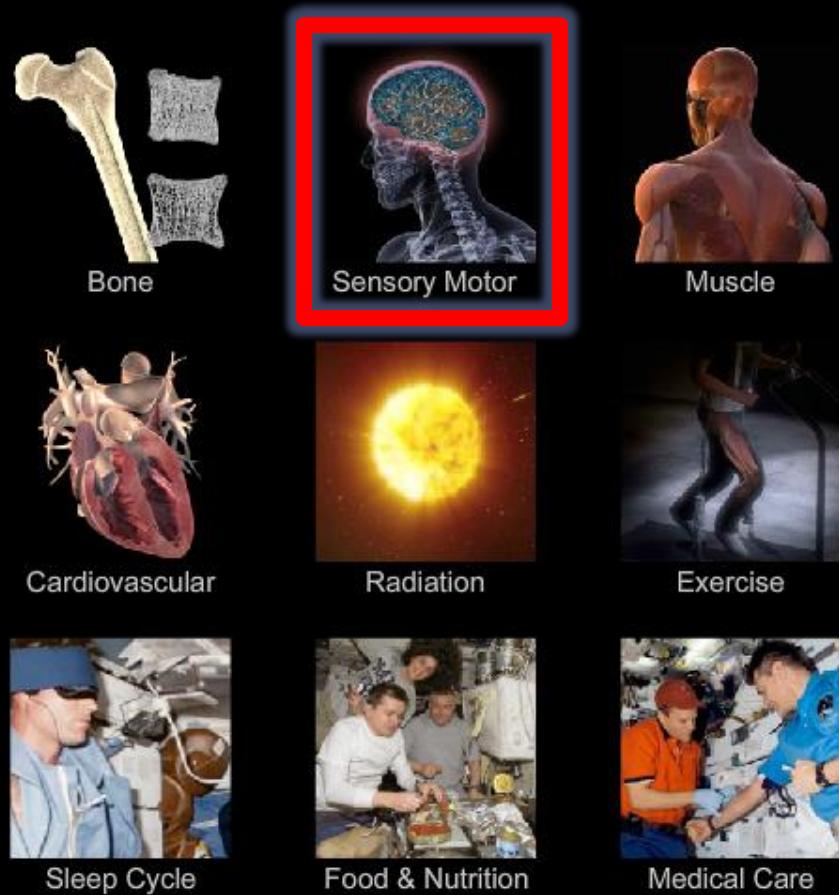
- Physiological challenges to astronauts are *substantial*, especially outside of Low Earth Orbit. For example...
- Muscle Density & Function
- Bone Health
- Ionizing (High Energy) Radiation
  - Filtered by Earth's magnetic field
  - Galactic cosmic radiation
    - Bare atomic nuclei (as heavy as iron atoms) traveling at speed of light
    - Mars mission may expose ~90x the max *annual* dose recommended on Earth
    - Cataracts??
  - Solar flares
    - Can produce unexpected, lethal radiation spikes





# Background: *Physiological Challenges*

- **Physiological challenges** to astronauts are *substantial*, especially outside of Low Earth Orbit. For example...
- **Vision Issues**
  - For >40 yrs, anecdotal reports indicated VA impairments w/ spaceflight
  - NASA survey (n > 300) showed **29%** of short- & **60%** of long-duration (ISS) crew experienced “degradation” of dist or near VA
    - Some ISS cases did not resolve post-flight
  - In 2005, a more serious disorder was identified. Termed:
    - Vision Impairment Intracranial Pressure (VIIP) --or--
    - Microgravity Ocular Syndrome (MOS)





# VIIP/MOS Clinical Findings





# VIIP/MOS: Clinical Findings

To date, 24 USOS ISS long-duration spaceflight astronauts have developed some or all of the following findings:

Ocular

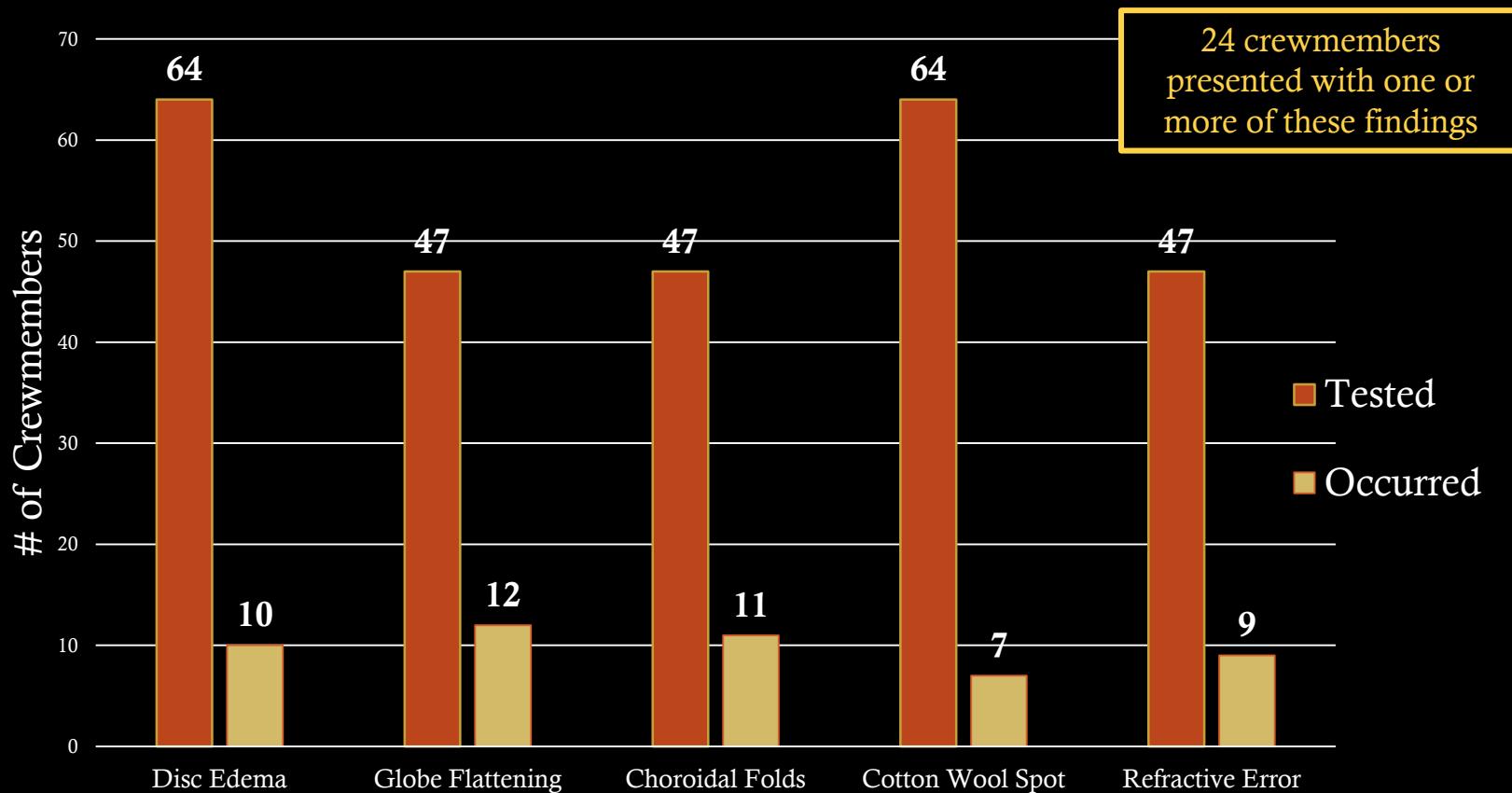
- Hyperopic shift
- Globe flattening
- Choroidal folds
- Cotton wool spots
- Optic disc edema
- Optic nerve sheath distention

*ALL are potential signs of elevated intracranial pressure (ICP)*

- Mildly elevated post-flight intracranial pressure
  - 21 - 29 cm H<sub>2</sub>O range
    - Upper limit of normal: ~20 cm H<sub>2</sub>O
    - Gray zone: 20.1 – 24.9 cm H<sub>2</sub>O



# USOS Individuals w/ VIIP/MOS Findings: Expeditions 1-48

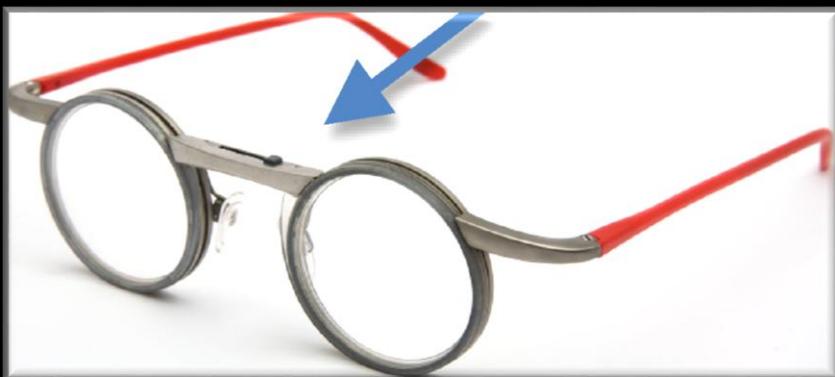


- ❖ Disc Edema = Modified Frisen Scale Grade  $\geq 1$  at first post-flight eye exam (via fundoscopy)
- ❖ Globe Flattening = A change compared to preflight (via MRI or ultrasound)
- ❖ Choroidal Folds = New or worsened compared to pre-flight (via OCT)
- ❖ Cotton Wool Spot = Presence in-flight or post-flight (via fundoscopy)
- ❖ Refractive Error = Change in cycloplegic (spherical) refraction  $\geq 0.75\text{D}$  from preflight to first post-flight eye exam



# Clinical Findings: *Hyperopic Shift*

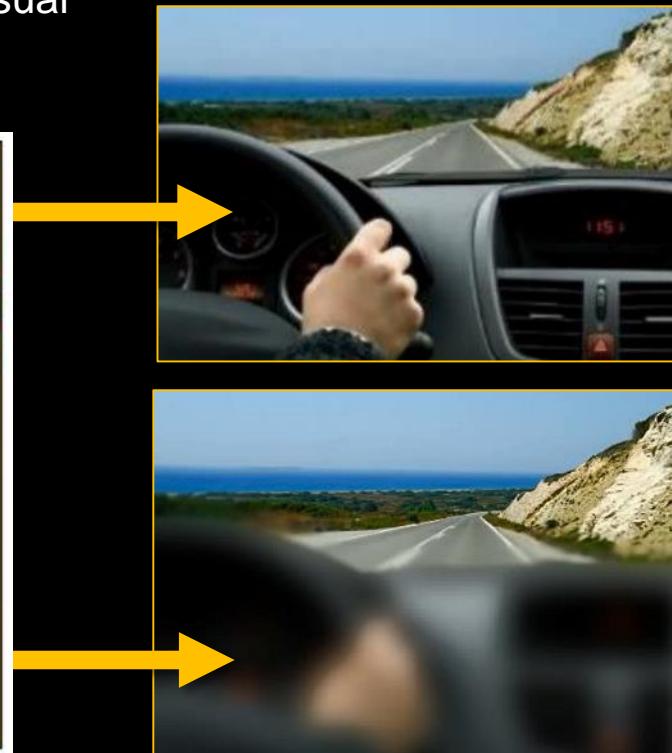
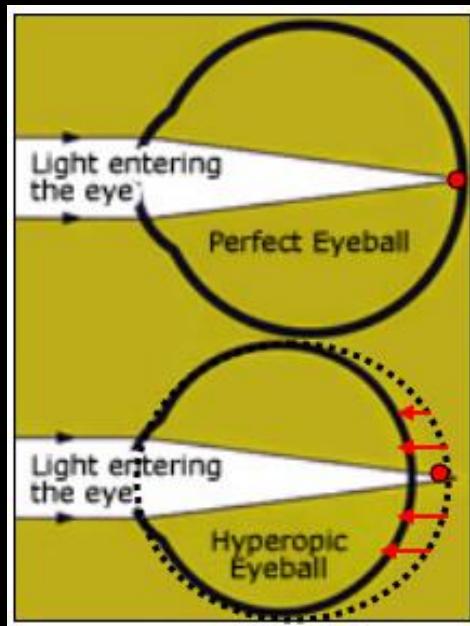
- Of the active astronaut population...
  - 80% wear vision correction (32% contact lenses)
  - Mean age = 47 yrs
  - Majority are presbyopic (i.e., a normal, age-related, progressively worsening inability to focus clearly on near objects)
- From postflight questionnaires (1989 - 2011): *29% of short-duration (Shuttle) & 60% of long-duration (ISS) mission astronauts report a subjective degradation in vision*, especially at near
  - Provided “Space Anticipation Glasses”





# Clinical Findings: *Hyperopic Shift*

- Subjective Degradation in Vision (cont):
  - Associated w/ *Hyperopic Shifts* in refractive error due to *Globe Flattening*
    - A 1 mm decrease in axial length will produce a ~2.7 diopter hyperopic shift
    - Largest shift to date is +1.75 diopters
    - In presbyopes: Typically decreases near visual acuity (VA), but leaves distant VA intact



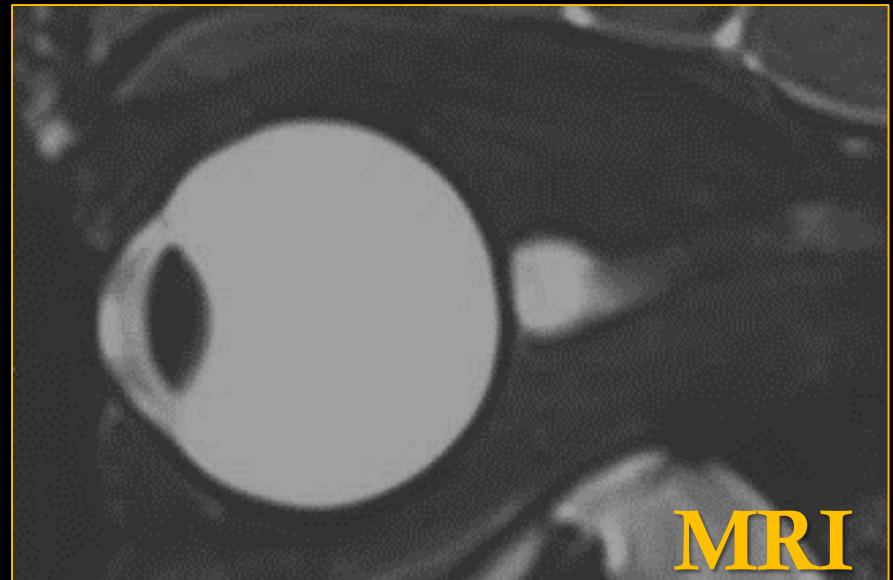


# Clinical Findings: *Globe Flattening*

- Case Example:

- Male, mid 40s at time of flight
- No significant PMH/PSH/PFH
- No meds
- Normal BP (118/64)
- Normal lipids
- ECG Stress test normal
- w/  $\text{VO}_2$  max of 51ml/kg

- *Terrestrially: Globe flattening associated w/ papilledema (i.e., disc edema 2° to increased intracranial pressure); typically bilateral*



Pre-flight

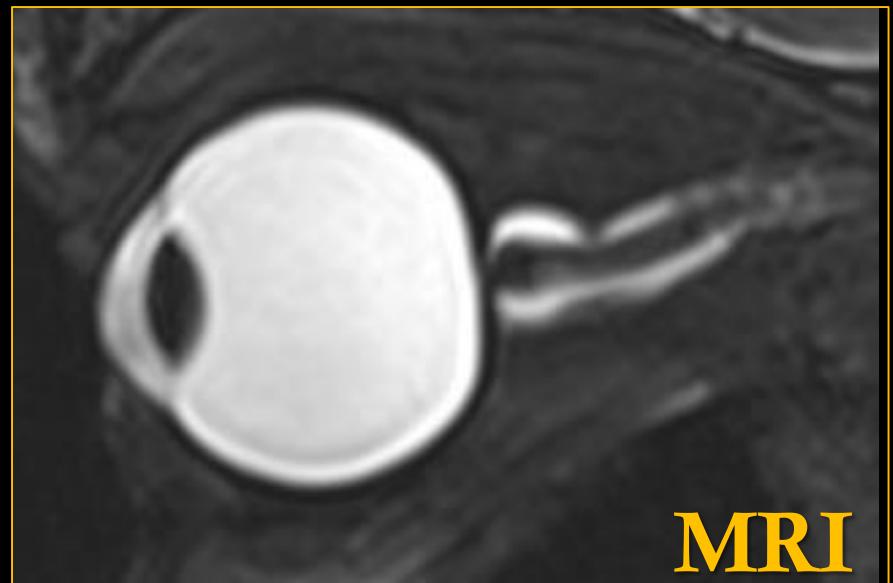


# Clinical Findings: *Globe Flattening*

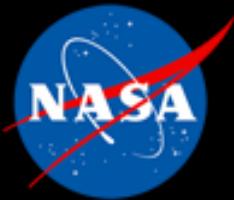
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6 days post-flight

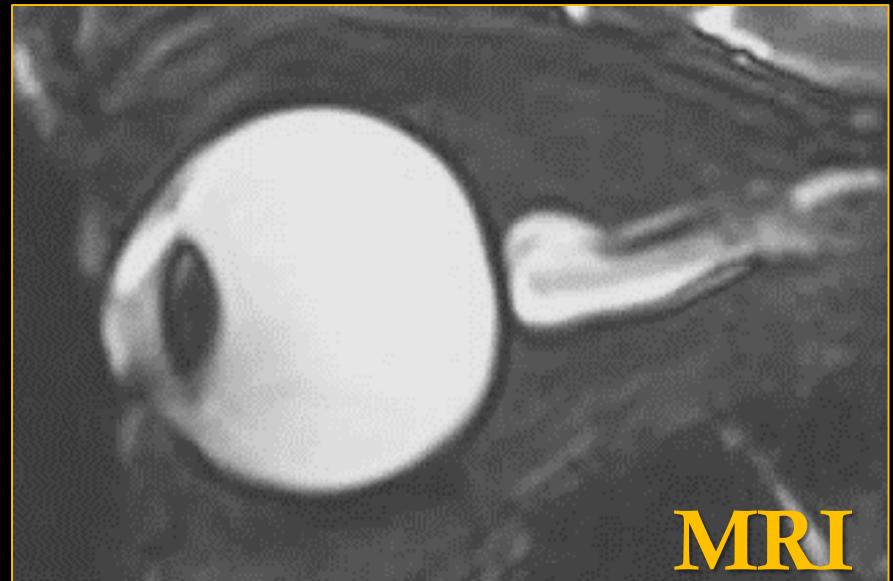


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1 year post-flight

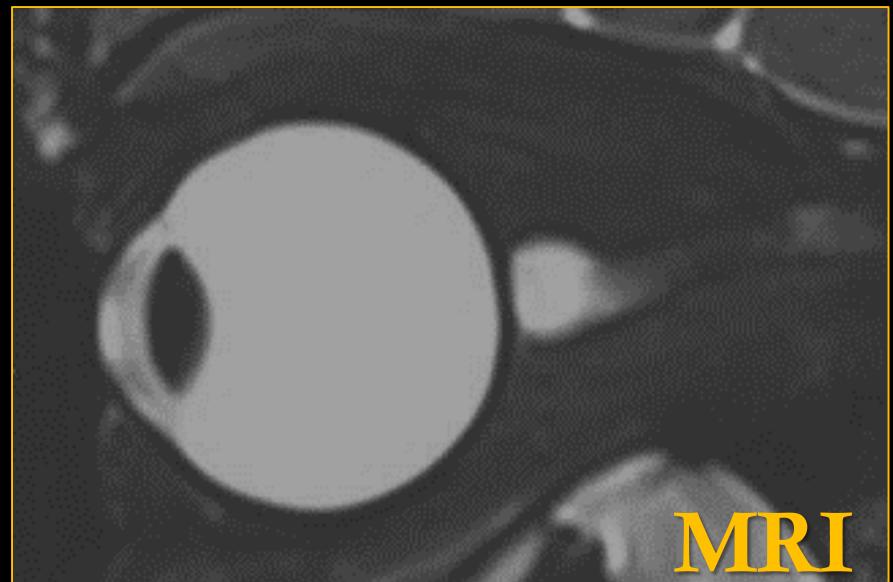


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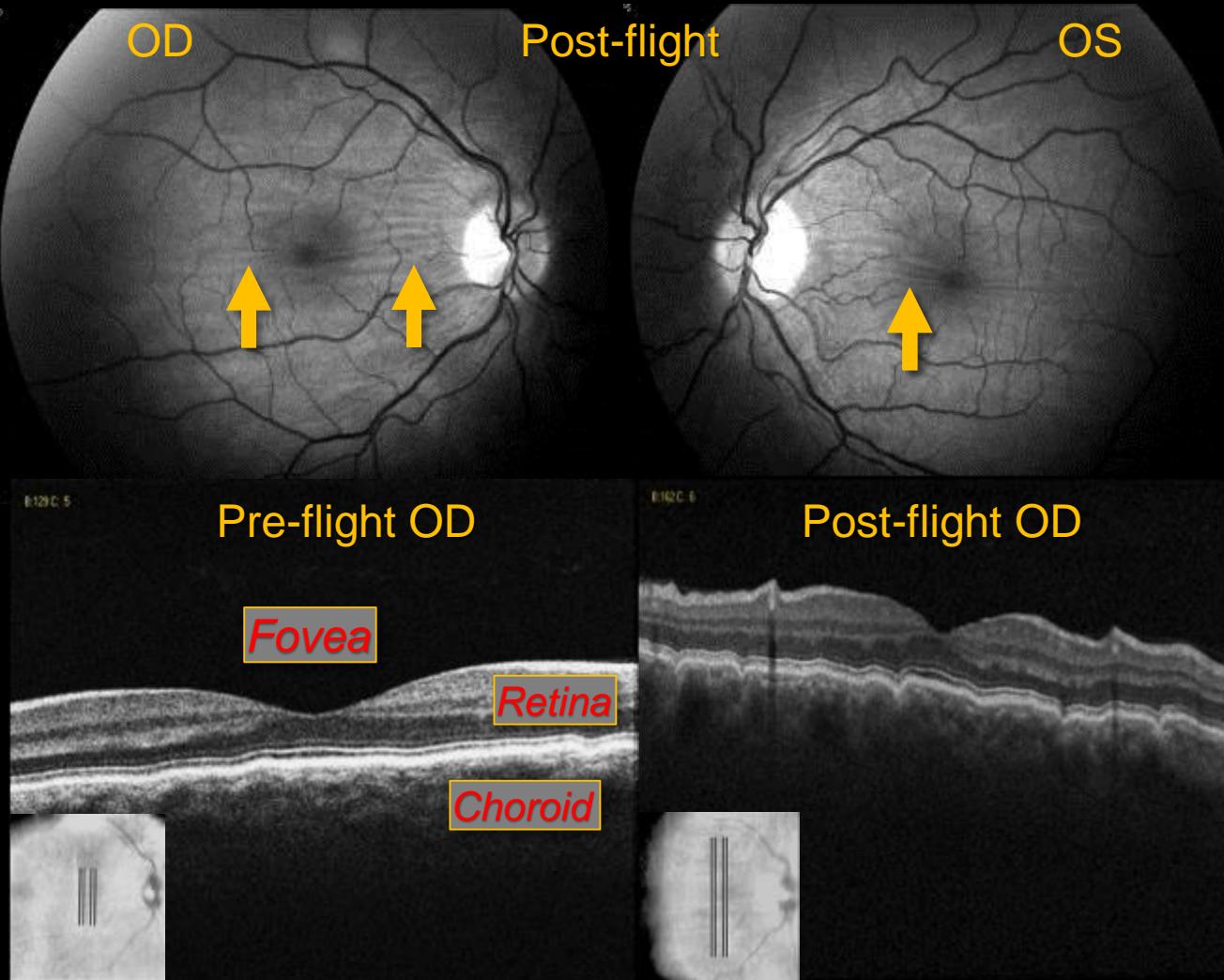
- *Terrestrially: Globe flattening associated w/ papilledema (i.e., disc edema 2° to increased intracranial pressure); typically bilateral*



Pre-flight



# Clinical Findings: *Choroidal Folds*



- Choroidal thickening due to vessel engorgement → induces choroidal (and sometimes retinal) folds
- Can resolve post-flight or can persist (for 5+ yrs)
- So far, no clinically-significant impact on BCVA
- *Terrestrially*: Assoc. w/ choroidal tumors, scleritis, retrobulbar mass, papilledema/IIH



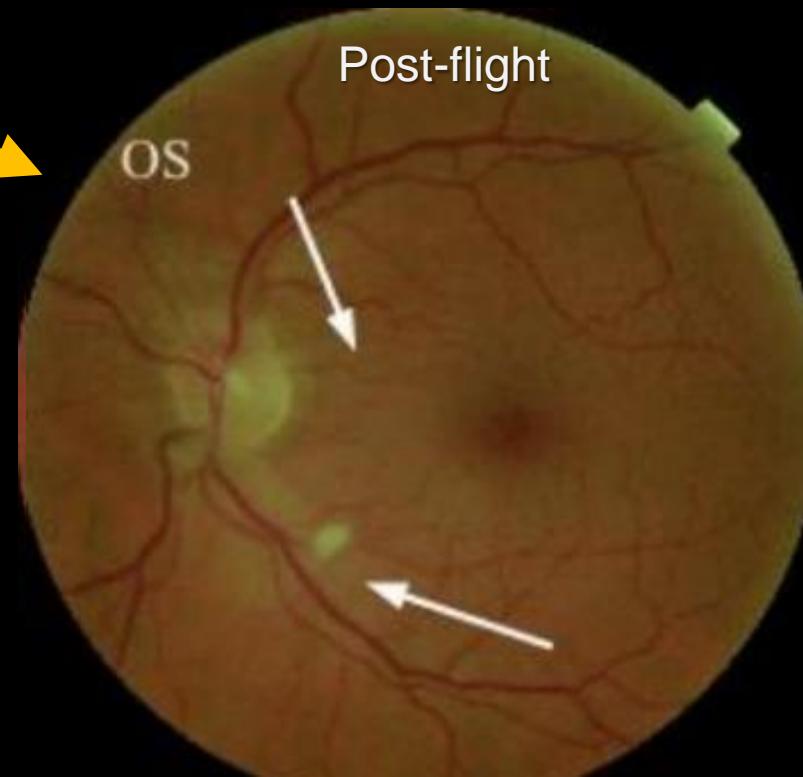
# Clinical Findings: *Cotton Wool Spots*

Posterior pole fundoscopic images  
OD & OS for two ISS crewmembers

- Top arrows: Choroidal folds
- Bottom arrows: Cotton wool spots

- Cotton wool spots
  - Abnormal retinal finding
  - Accumulations of axoplasmic material w/in retinal nerve fiber layer
  - Caused by ischemia → reduced axonal transport → swelling of axon → damaged nerve fibers
  - *Terrestrially*: Associated w/ diabetes, HTN, central retinal vein occlusion

## Example 1





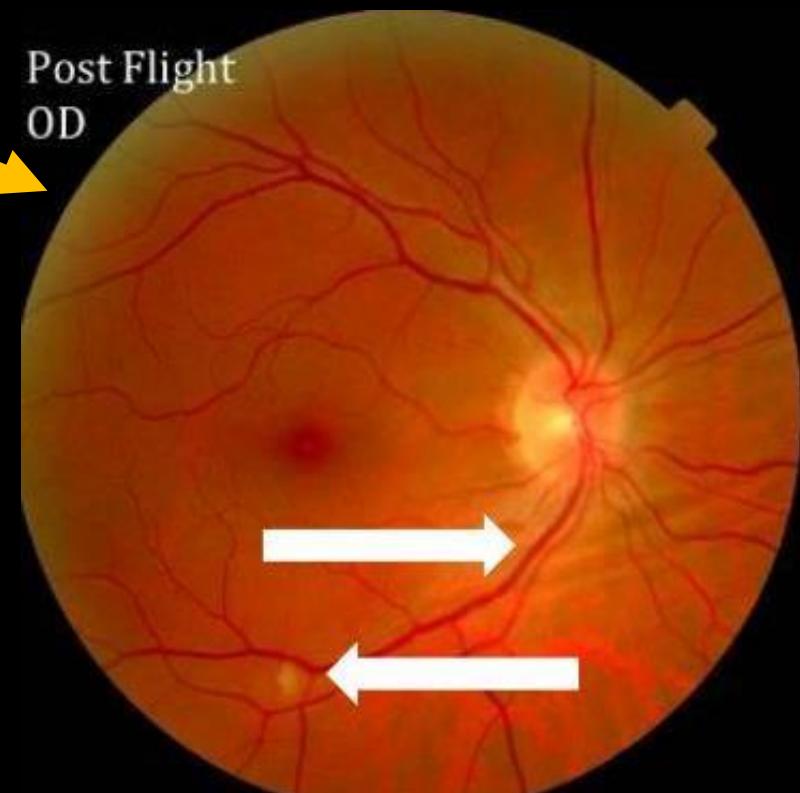
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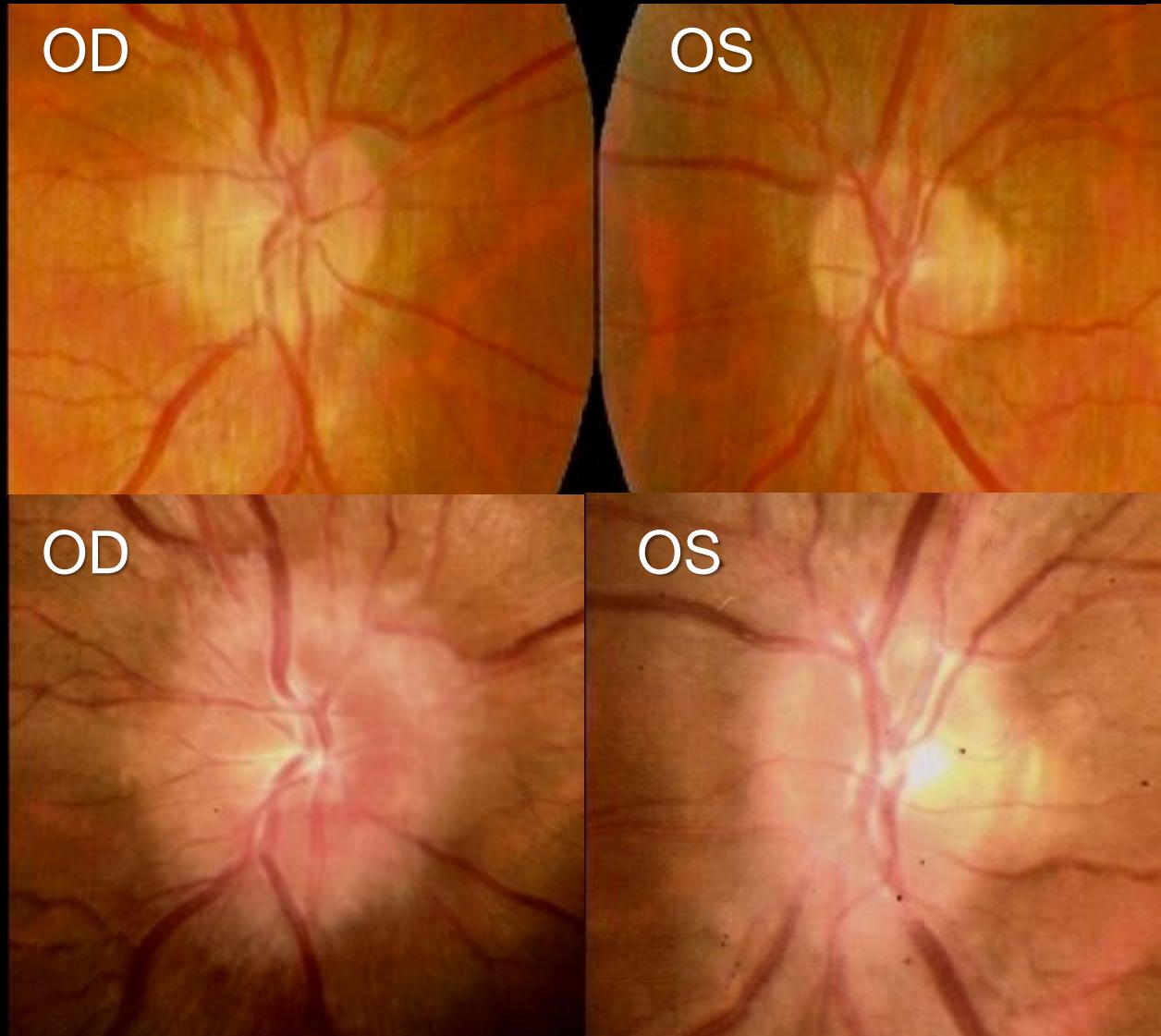
*Example 2*



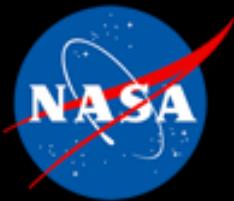


# Clinical Findings: *Optic Disc Edema*

Pre-flight fundoscopic images of the right (OD) & left (OS) optic discs

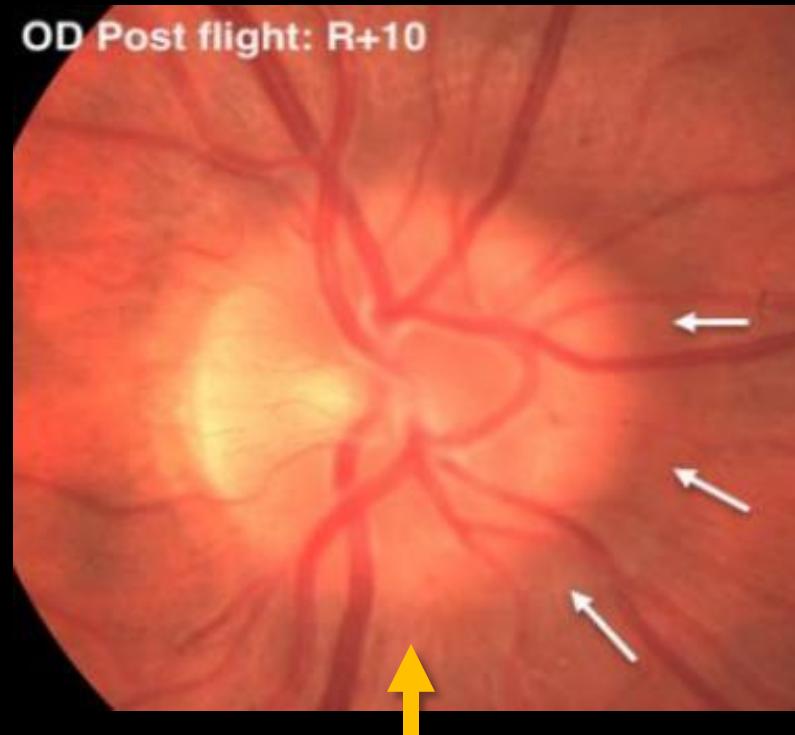


Post-flight images of optic discs, showing *Grade 3 edema* OD & *Grade 1 edema* OS



# Clinical Findings: *Optic Disc Edema*

- **Terrestrially:** Optic disc edema is associated with:
  - Unilateral: Optic neuritis, optic neuropathy, retinal artery/vein occlusion
  - Bilateral: Increase in ICP...
    - IIH ( $\rightarrow$  “papilledema”)
    - Intracranial mass
    - Cerebral edema
    - Increased CSF production
    - Decreased CSF absorption
    - Obstructive hydrocephalus
    - Venous outflow obstruction
  - Typically reduces VA, enlarges blind spot, causes relative afferent pupillary defect & color impairment



Fundoscopic image of optic disc OD, 10 days after return to Earth

- Arrows: “C” shaped halo of edema

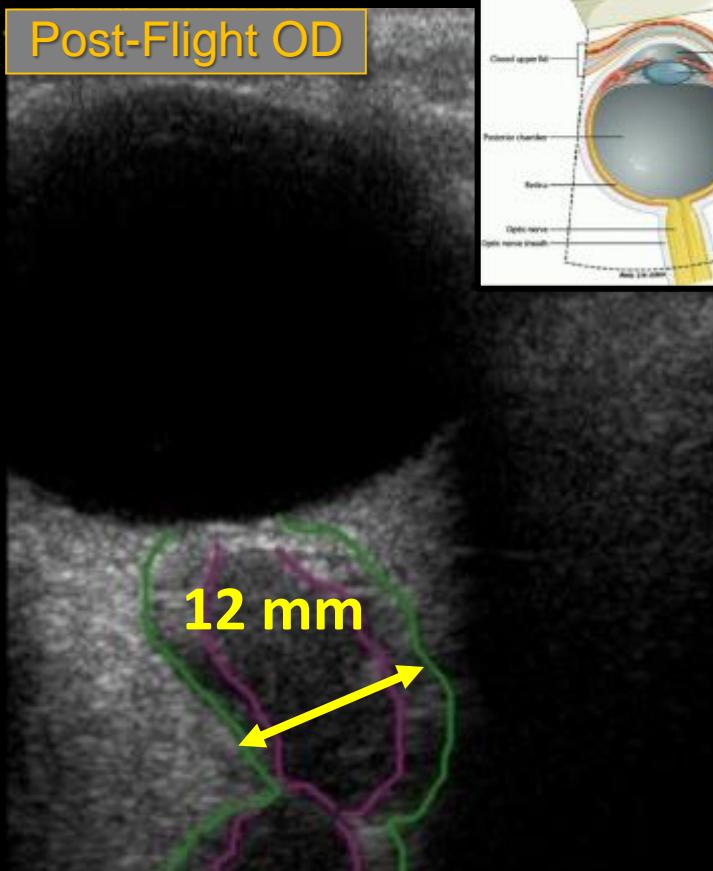


# Clinical Findings: *Optic Nerve Sheath Distention*

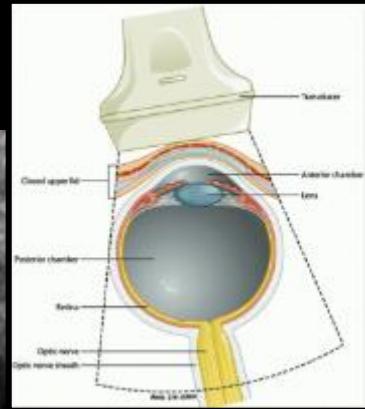
Post-flight ultrasound image of globe, optic nerve (ON; purple), and optic nerve sheath (green). Showing:

- ON Sheath distention
- ON tortuosity

Post-Flight OD



- **ON Sheath *terrestrially*:**
  - Normal diameter (ONSD)  
 $< 5.9$  mm
  - Enlargement typically associated w/ increased ICP





# Common Characteristics of the Cases





# Common Characteristics of the Cases

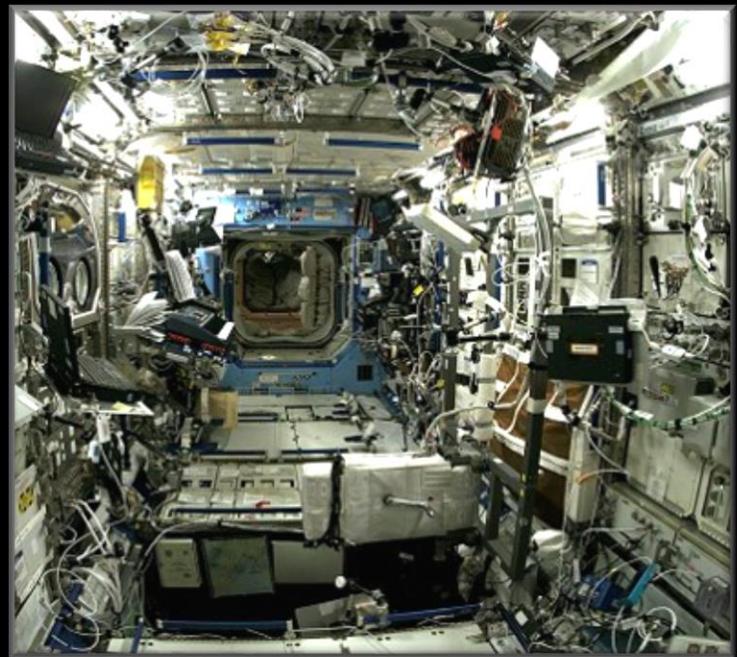
- Almost all were *~6 month duration ISS mission crewmembers*
  - One short-duration case w/ subtle disc edema (discovered retrospectively)
  - Severity related to flight duration?
    - What about a *3-yr Mars mission??*
- All had normal pre-flight eye exams
- Normal past medical history:
  - *Negative* for systemic disease
  - None had used medications before/during their mission that could increase ICP (e.g., vitamin A, tetracycline, corticosteroids, or nalidixic acid)





# Common Characteristics of the Cases

- None complained of headaches, transient vision obscurations, double vision, pulsatile tinnitus, or vision changes during eye mvmnts (i.e., classic symptoms of idiopathic intracranial hypertension)
- None experienced loss in BCVA, color vision, or stereopsis
- OD affected more than OS *in all cases*. If only one eye affected, always OD
- ISS cabin
  - Normal pressure & oxygen
  - Elevated CO<sub>2</sub>
    - ~0.33-0.5% avg, w/ avg peak ~0.7%
    - 10x terrestrially: ~0.03-0.04%





# Why is this Happening?





# Why is this Happening?

- Terrestrially → Fluid is pulled downward by gravity (i.e., hydrostatic pressure)
- Microgravity → Fluid is free to uniformly distribute (i.e., hydrostatic pressure is eliminated)

Consider how hydrostatic pressure affects fluid/blood distribution in humans...

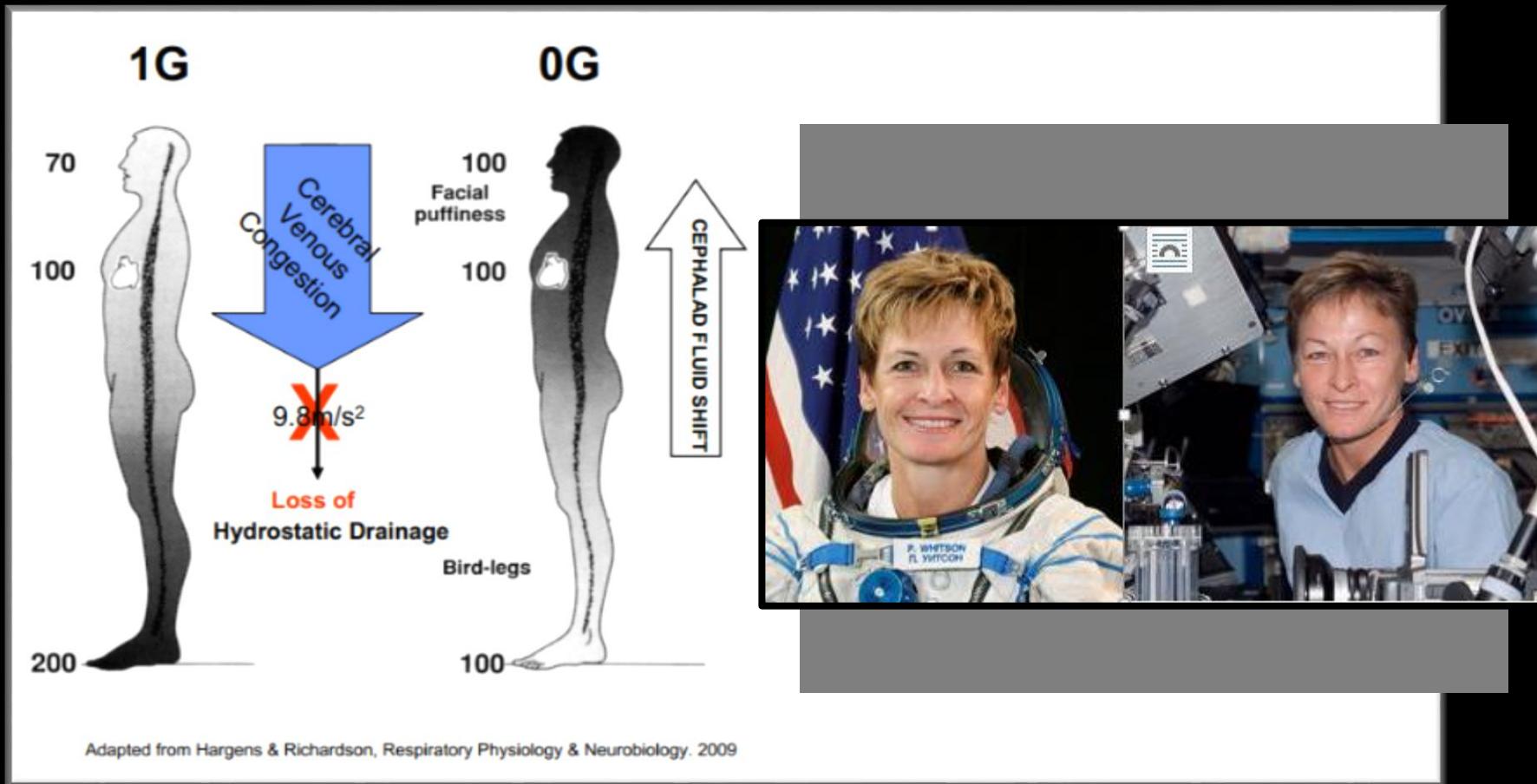
And what happens in its absence...





# Why is this Happening?

Microgravity → Cephalad fluid shift → Cerebral venous congestion

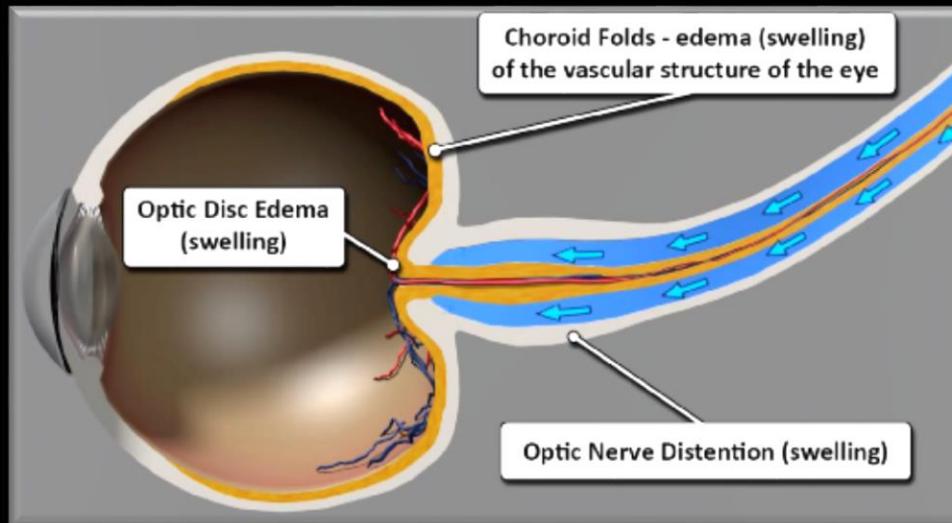




# Why is this Happening?

- Current Risk Statement:  
“Visual Impairment Intracranial Pressure” (VIIP)

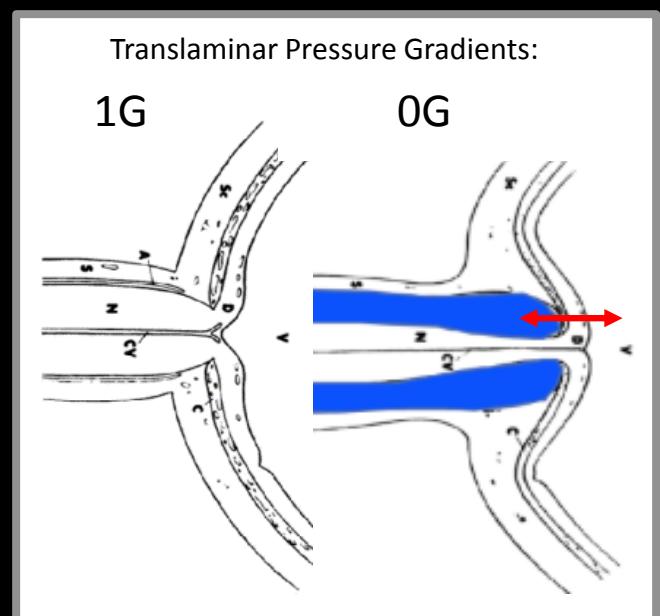
"Given that the microgravity environment causes cephalad fluid shift in astronauts, there is a probability that astronauts will have intracranial hypertension (IHT) to some degree, which if left untreated, could lead to deleterious health effects."





# Why is this Happening?

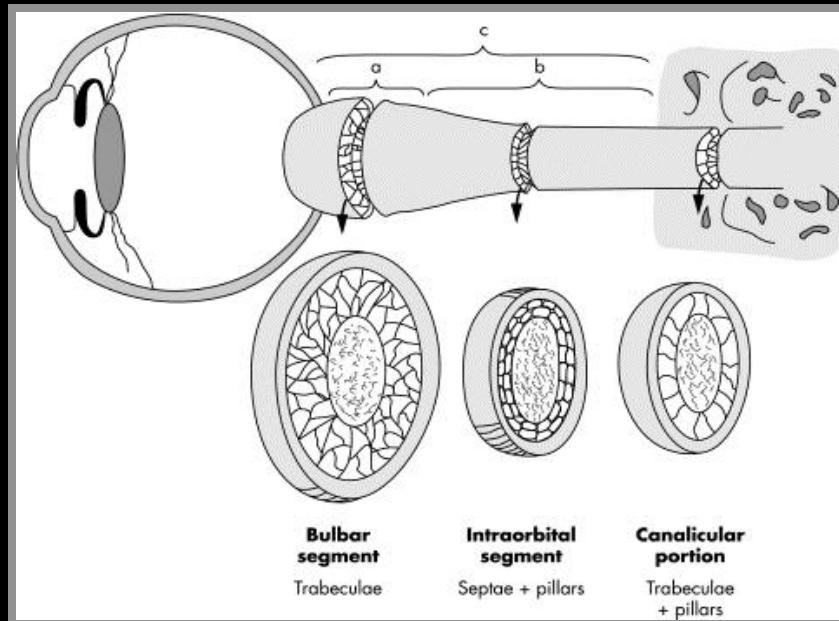
- Hypothesis #1: Increased intracranial pressure
  - The original theory, hence “Visual Impairment Intracranial Pressure”
  - Support:
    - Optic nerve edema & ONSD distention
    - Lateral & 3<sup>rd</sup> ventricle enlargement (like hydrocephalus) post-flight
    - Crowding of superior sagittal sinus post-mission
  - However:
    - Signs often unilateral & right-biased
    - If ICP increases, may increase only modestly
    - Globe flattening & choroidal folds can persist for years post-flight, despite a return to normal ICP

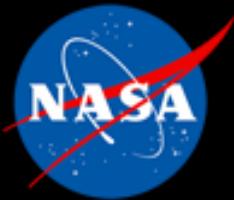




# Why is this Happening?

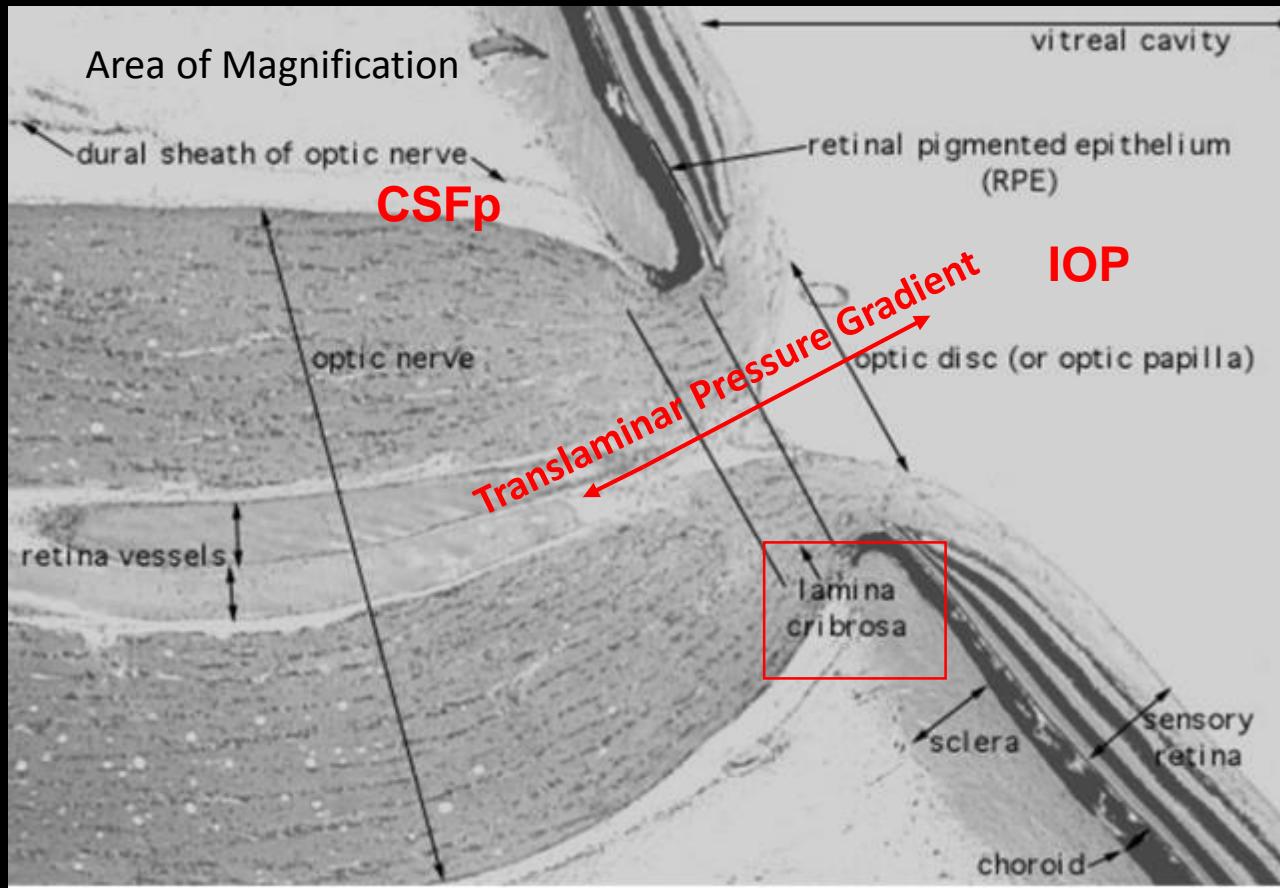
- Hypothesis #2: This is a local ocular eye problem
  - CSF cul-de-sac bathing ON might act as one-way valve for CSF flow during spaceflight → may increase local ICP around ON





# Why is this Happening?

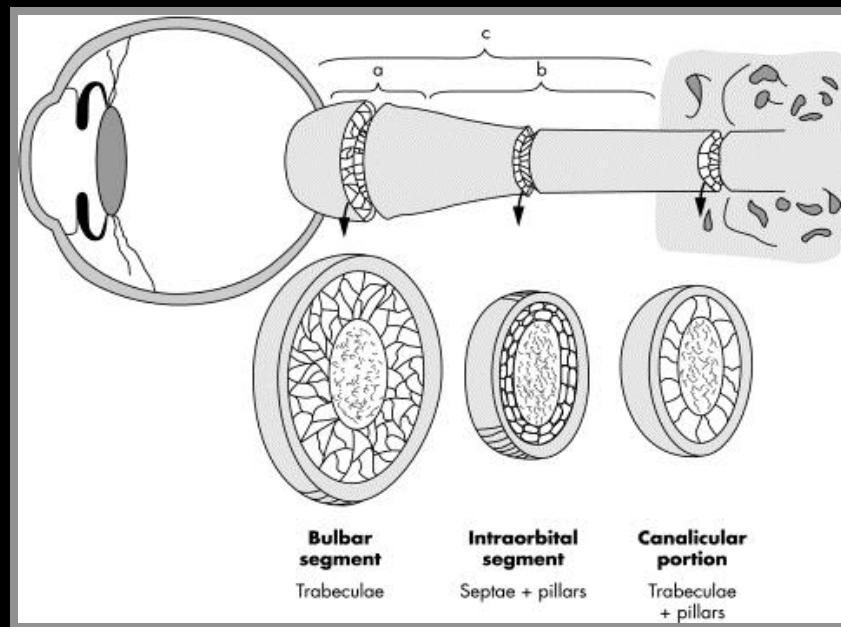
- Hypothesis #3: Slight IOP reduction + slight ICP increase
  - Variation of original VIIP theory (i.e., ↑ ICP)





# Why is this Happening?

- Hypothesis #4: Individual anatomical or genetic factors
  - For example: VIIP may be associated w/ atypical folate-dependent 1-carbon metabolic pathway in some astronauts
    - May increase local toxin concentration w/in ON sheath





# Why is this Happening?

- Hypothesis #5: Vessel congestion places local pressure in choroid & around optic nerve (“Circle of Zinn-Haller” theory)

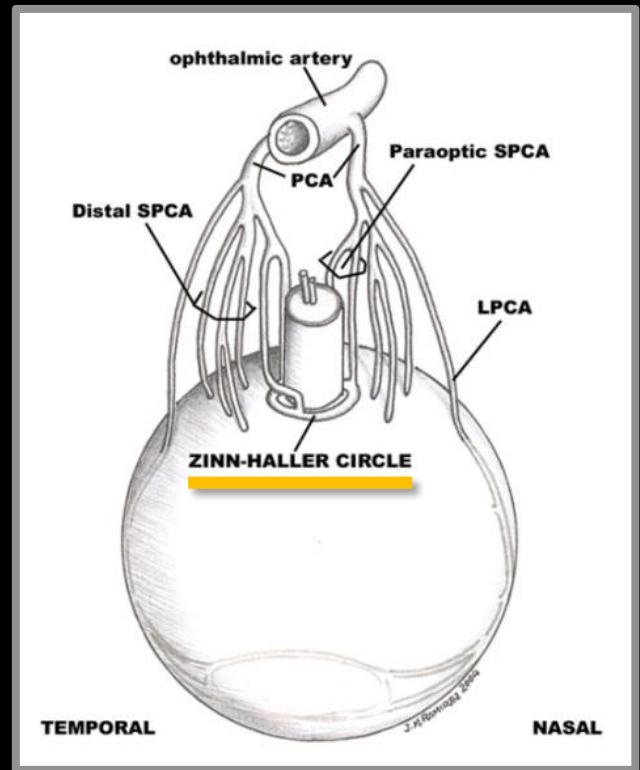
In  $\mu$ Gravity, head venous pressure  $\approx 15-20$  mmHg  
(vs. standing terrestrially  $\approx -20$  mmHg)



Choroid engorges & thickens, even in non-VIIP cases



Choroidal blood supply forms an anastomosis around ON. If engorged & pressurized, may place *noose-like strain* around ON





# In-flight Exacerbating Factors??

## Resistive Exercise



## High Oral Sodium Intake

Prepackaged Foods...  
Up to 5000+ mg/day



## High CO<sub>2</sub>

~10x terrestrial levels



## In-flight Pharmaceuticals





# Medical Surveillance

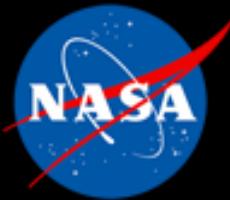




# Surveillance & Medical Data Collection

- 49 ISS expedition missions have been completed (since 2000)
- **Seminal VIIP case** occurred in **2005**
  - Choroidal folds & cotton wool spot OD; OS unremarkable
- Surveillance/medical data collection is ongoing and has evolved
  - Began *some* “VIIP” related testing in 2008 (w/ Exp 18)
  - Inconsistent testing until Feb 2010 (Exp 23) when standardized medical monitoring (i.e., “**Eye MED B**”) came into effect





# Surveillance & Medical Data Collection

## Terrestrially (pre- & post-flight)

- 3T MRI – Special “NASA Astronaut” protocol
- **Comprehensive eye exam. *Highlights:***
  - Refraction (manifest & cycloplegic); Amsler
  - Threshold VFs; Contrast sensitivity
  - Optical biometry; Applanation tonometry
  - Optical Coherence tomography (OCT)



## On-Orbit

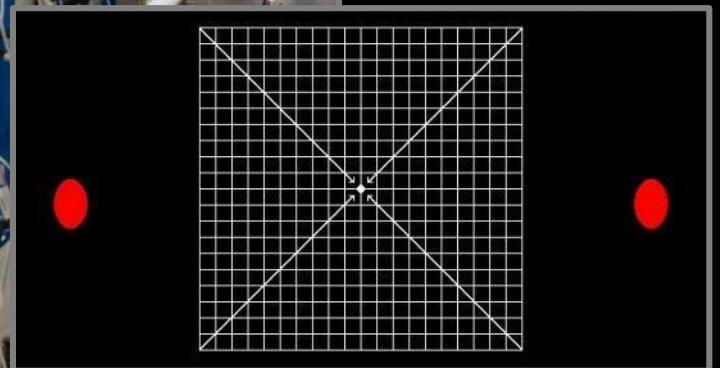
- Visual Acuity (Dist & Near)
- Amsler Grid
- Vision Questionnaire
- Ocular Ultrasound
- Fundoscopy
- OCT
- Tonometry (when clinically indicated)





# Surveillance & Medical Data Collection

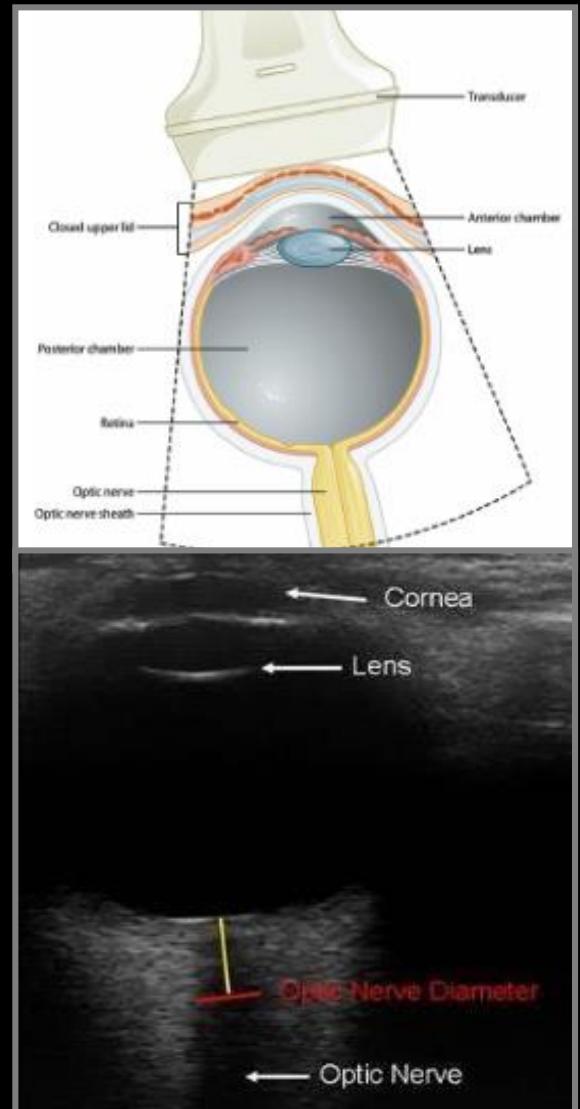
## On-orbit Visual Acuity & Amsler Grid





# Surveillance & Medical Data Collection

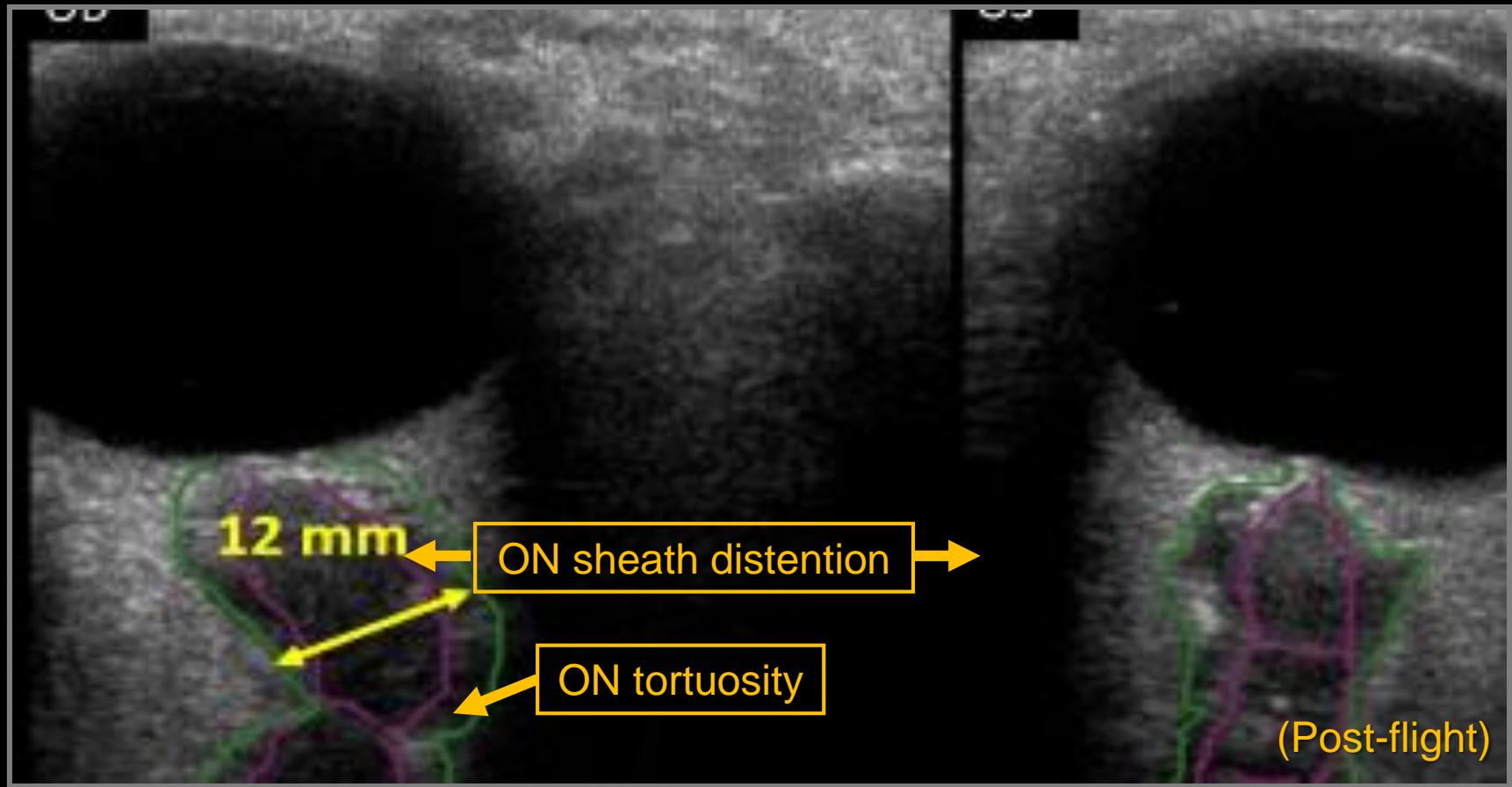
## On-orbit Ultrasound Imaging





# Surveillance & Medical Data Collection

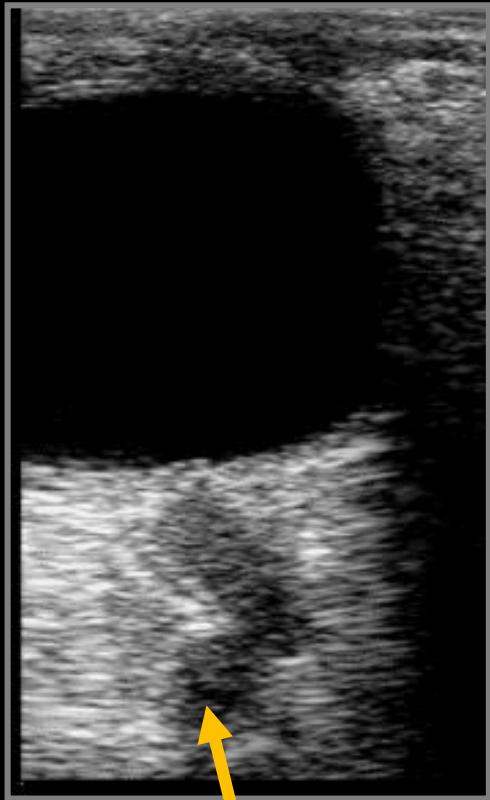
## On-orbit Ultrasound Imaging



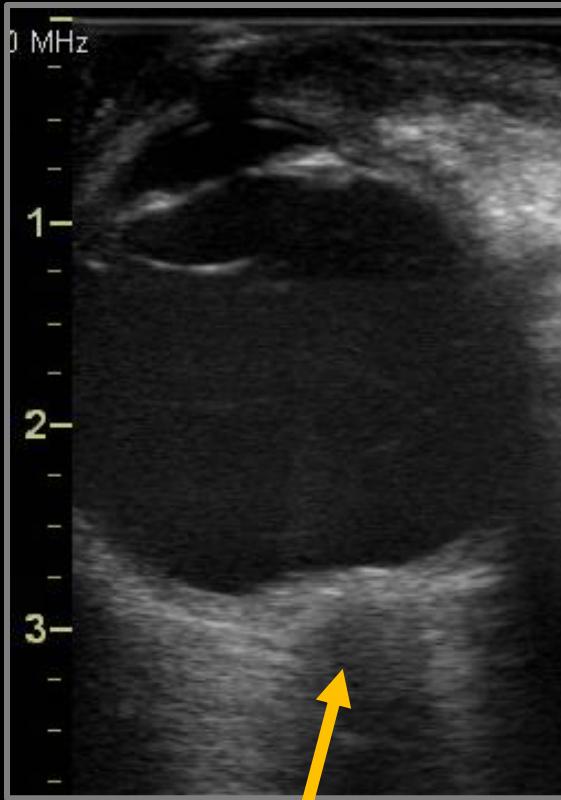


# Surveillance & Medical Data Collection

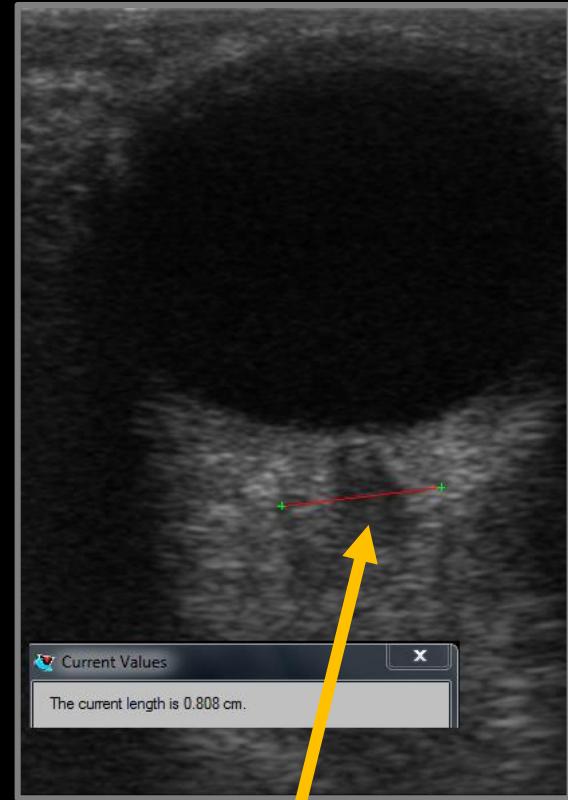
## On-orbit Ultrasound Imaging



ON tortuosity



Elevated optic disc

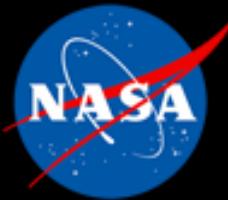


ON sheath distention



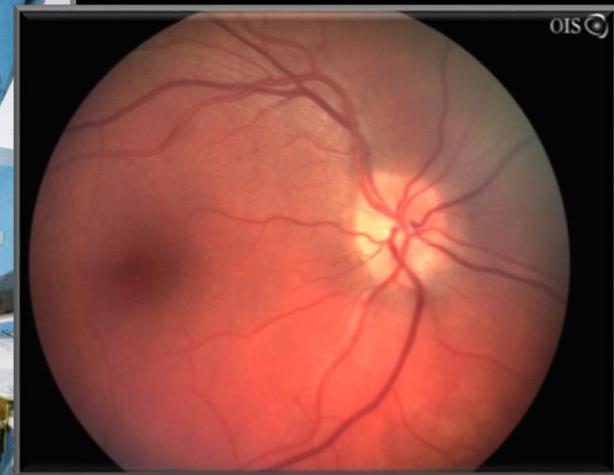
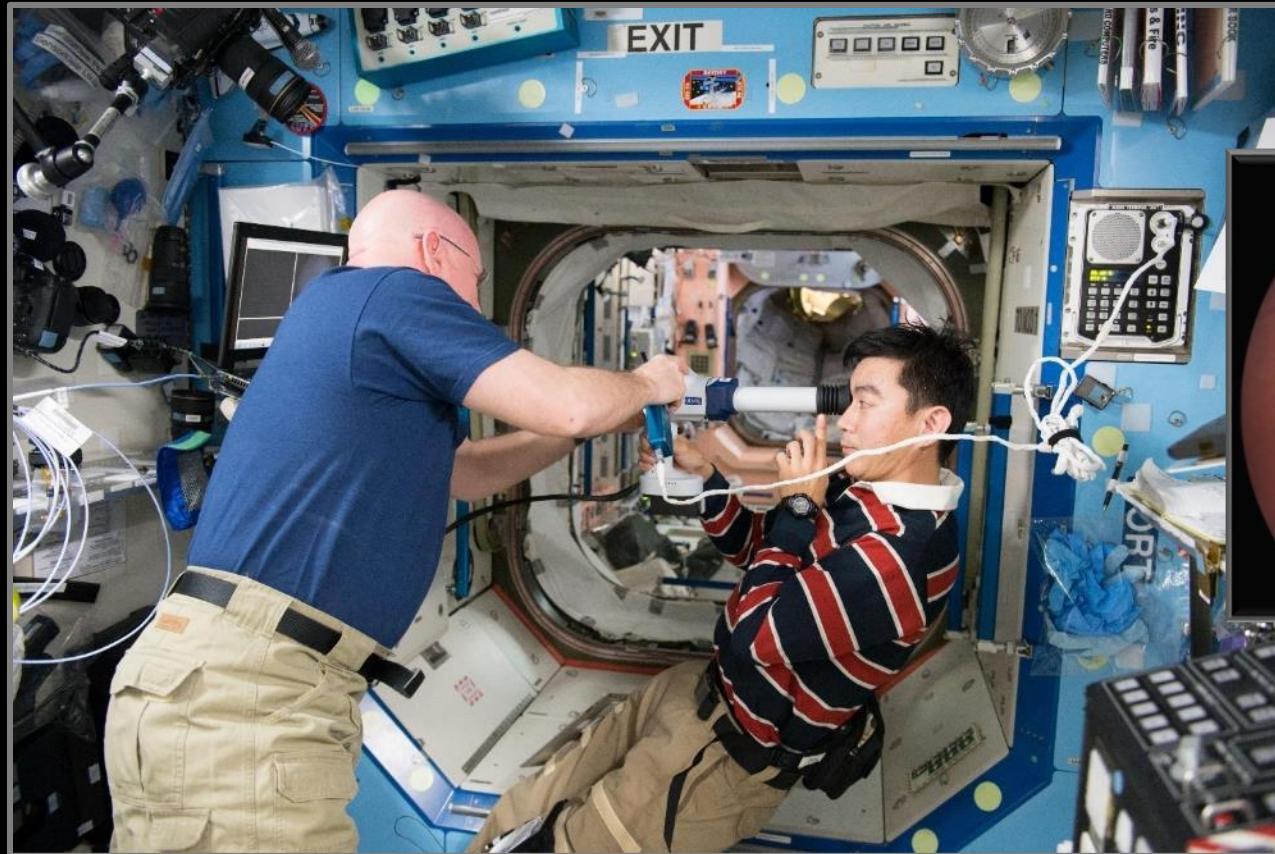
Current Values

The current length is 0.808 cm.



# Surveillance & Medical Data Collection

## On-orbit Fundoscope





# Surveillance & Medical Data Collection

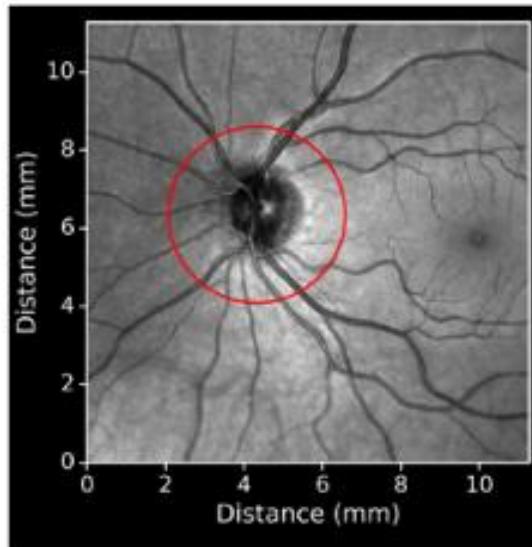
On-orbit Optical Coherence Tomography (OCT)



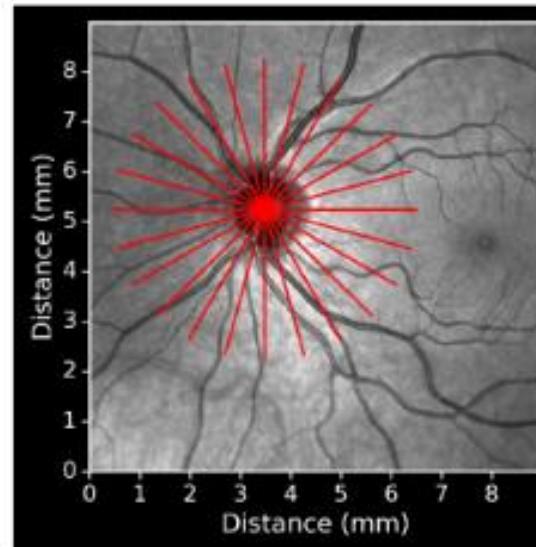


# Nominal OCT Protocol

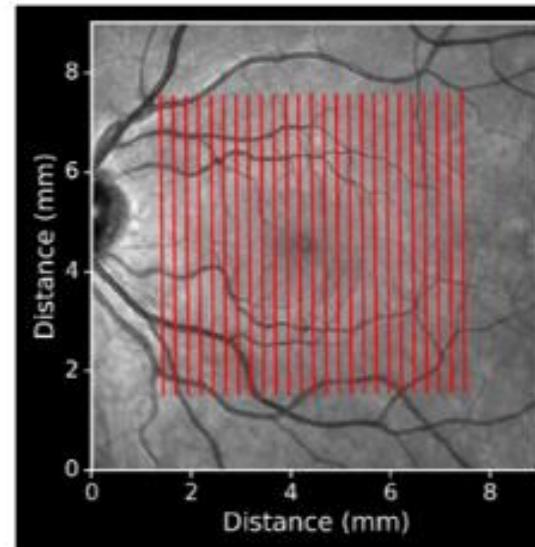
**Circular ONH Scan**



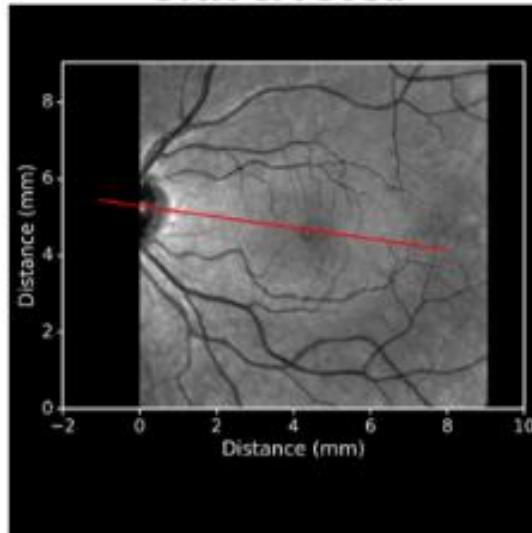
**Radial ONH Scan**



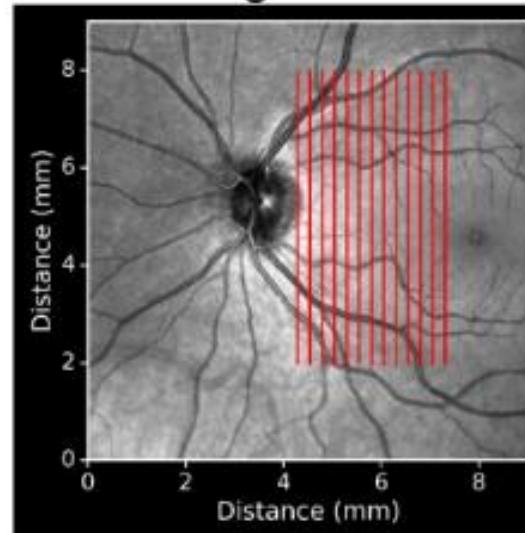
**Vertical Macula Scan**



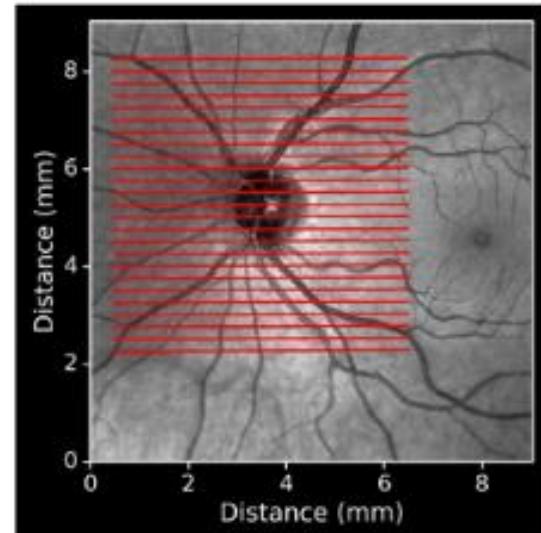
**Single Scan through  
ONH & Fovea**

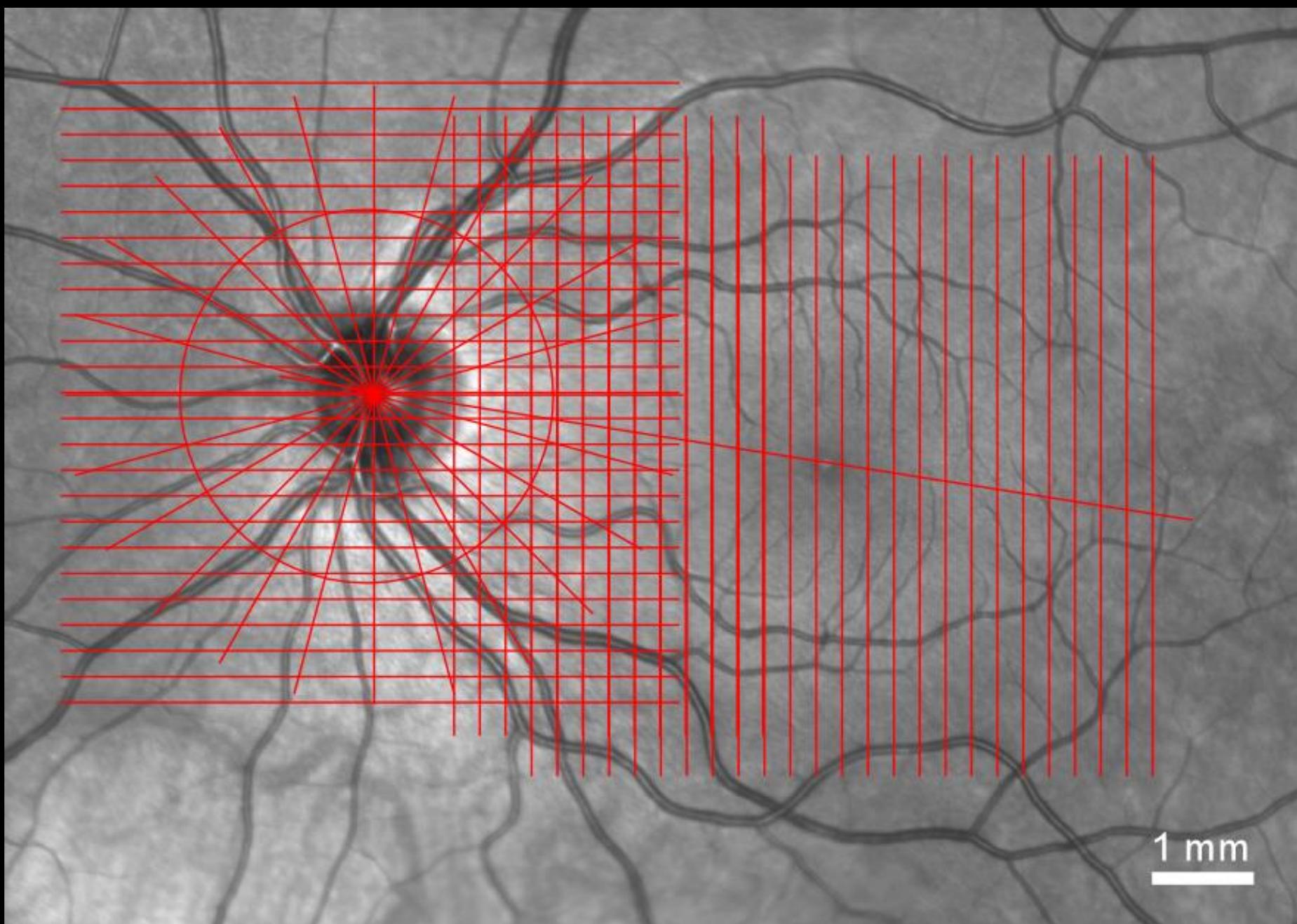


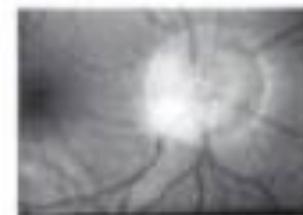
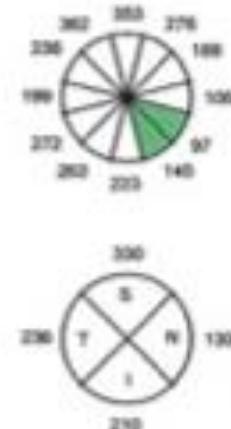
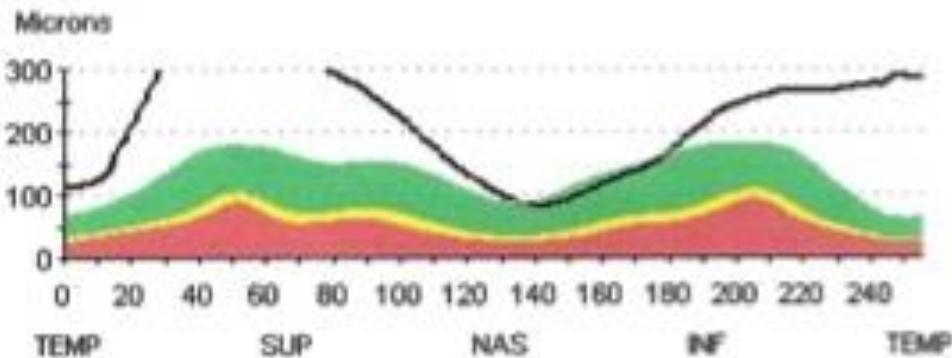
**Vertical Scan Between  
Disk Edge & Fovea**



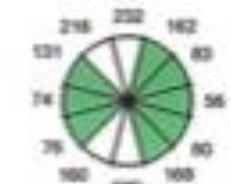
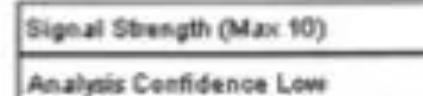
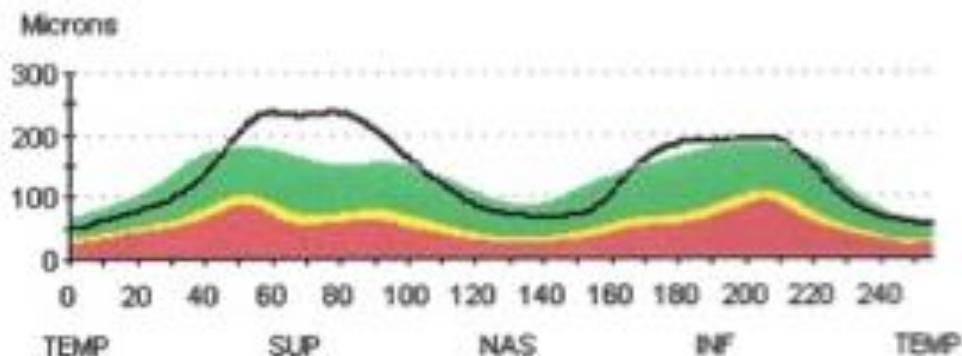
**Horizontal ONH Scan**



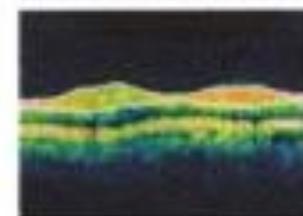
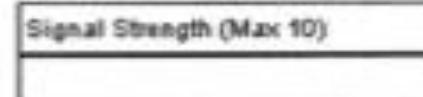
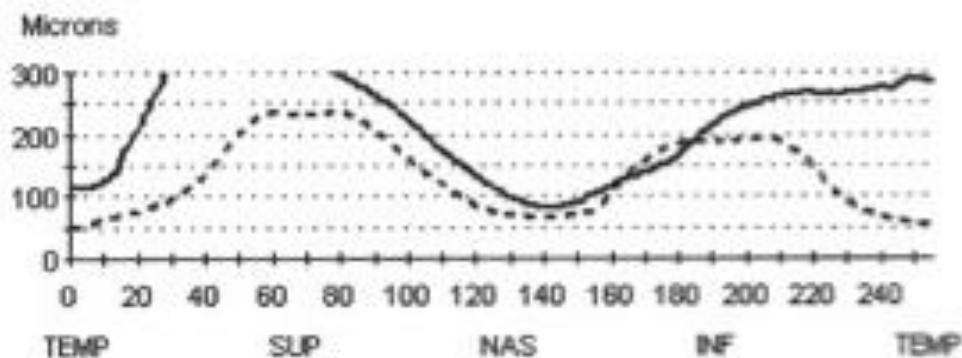




OD



OS

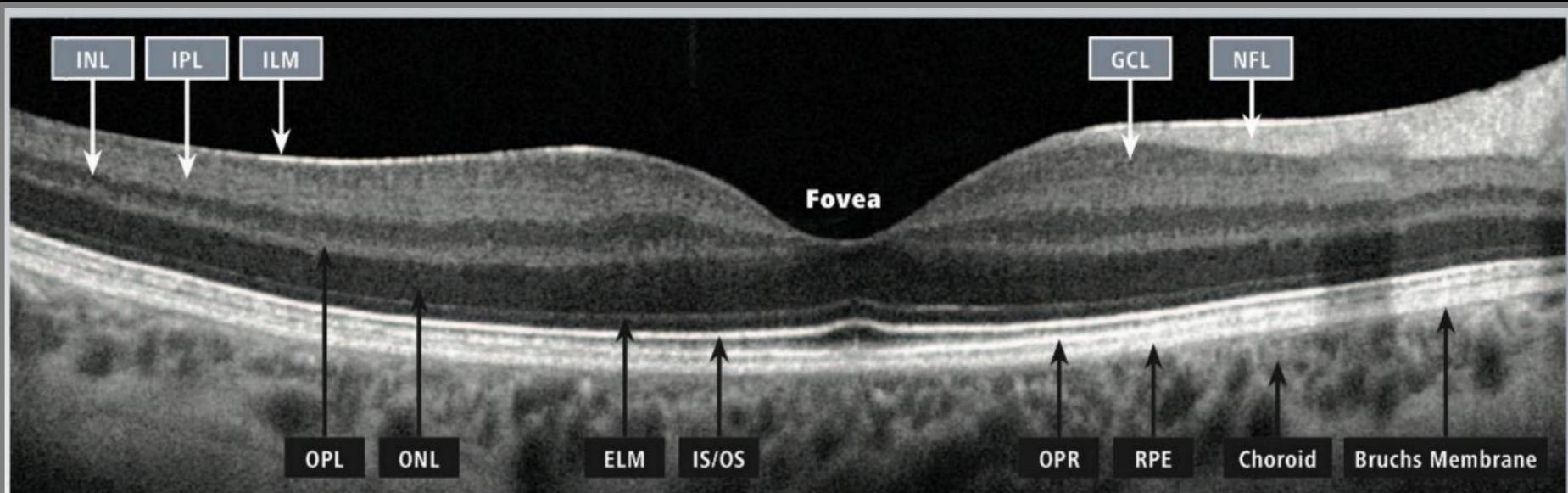


Post-flight OCT scan showing RNFL thickening consistent w/  
observed optic disc edema OU



# Surveillance & Medical Data Collection

## On-orbit Optical Coherence Tomography (OCT)



ILM: Inner limiting membrane  
IPL: Inner plexiform layer  
INL: Inner nuclear layer  
OPL: Outer plexiform layer  
ONL: Outer nuclear layer

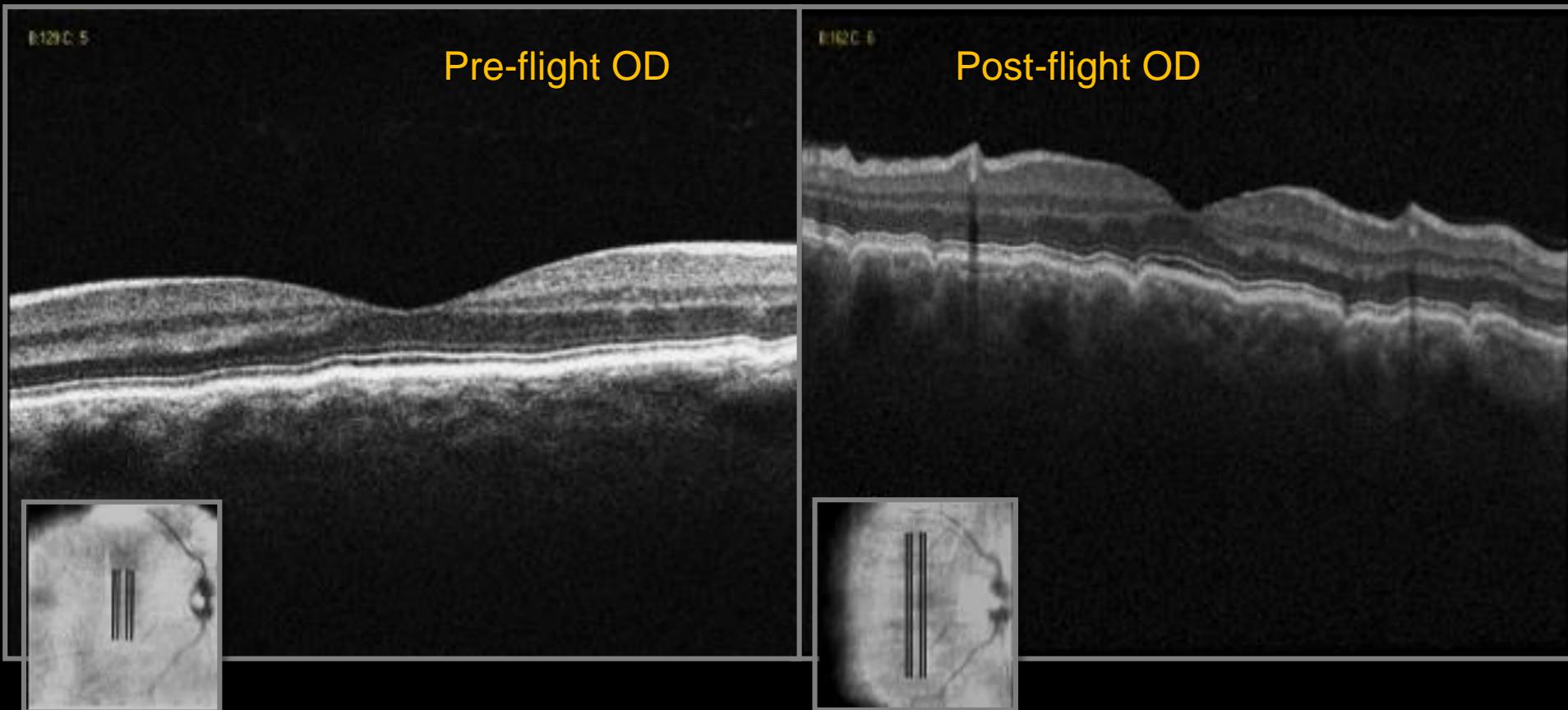
ELM: External limiting membrane  
IS/OS: Junction of inner and outer photoreceptor segments  
OPR: Outer segment PR/RPE complex

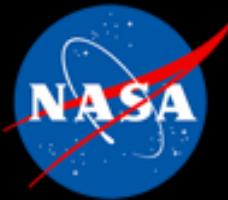
NFL: Nerve fiber layer  
GCL: Ganglion cell layer  
RPE: Retinal pigment epithelium + Bruch's Membrane



# Surveillance & Medical Data Collection

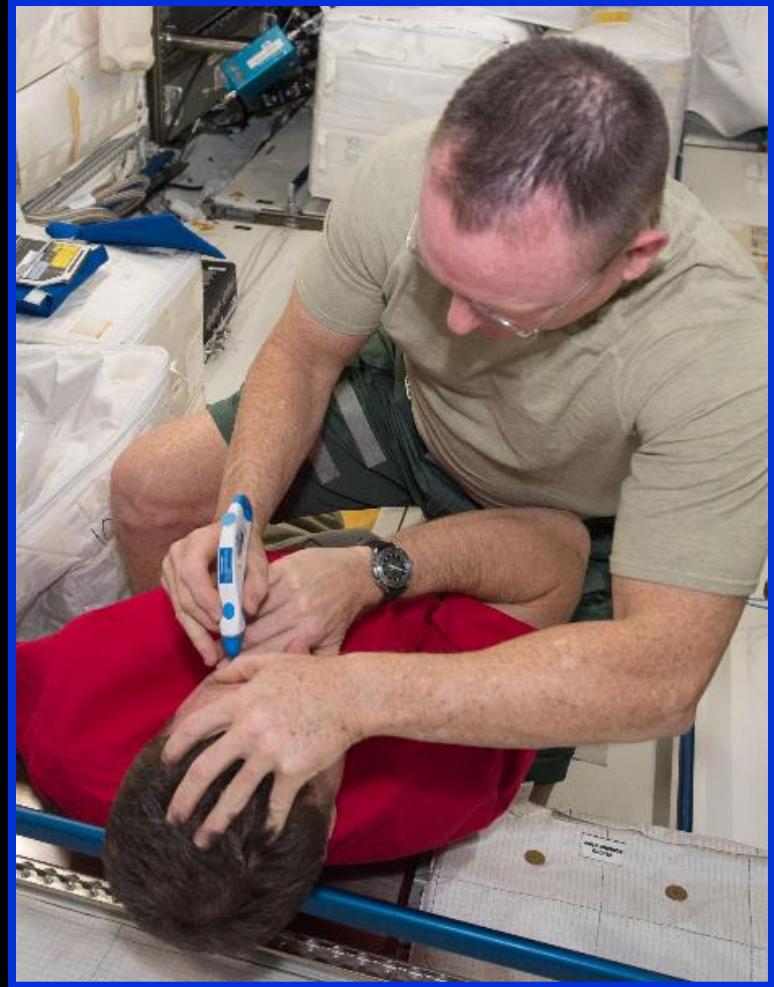
## On-orbit Optical Coherence Tomography (OCT)





# Surveillance & Medical Data Collection

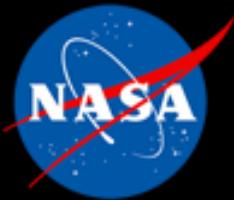
## On-orbit Tonometry





# Clinical & Research Update

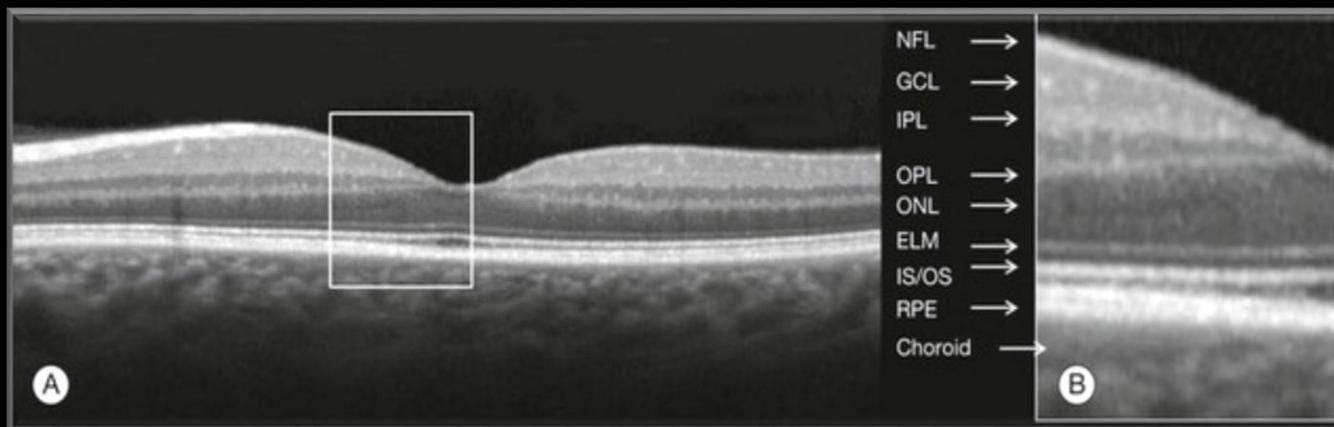




# Clinical Update: Feb17

## *Ongoing clinical work*

- Correlation between “*Form & Function*”: RNFL thickness changes (OCT) and their impact on visual sensitivity (VF)
- Correlations between VIIP/MOS signs and:
  - Subcortical white matter hyperintensities (WMH) found on MRI
  - Cardiovascular parameters (e.g., general fitness levels)
- Evaluation of next-generation OCT (“OCT2”): Will it enhance on-orbit imaging/data acquisition?





# What We Are Watching Coming From Our Research Colleagues

- **Ocular Health Study & Fluid Shifts Study**
  - Both finish data collection in Summer 2017
- Clinical relevance of **MRI-based findings**
- Implementation of **direct ICP measures** (pre- & post-mission)
- Correlation btwn **VIIP/MOS & CO<sub>2</sub>** using **HDT (EnviHab)**





# What We Are Watching Coming From Our Research Colleagues

- **Fluid Shifts Study:** OCT scan w/ lower body negative pressure
  - Not your typical clinical environment...!





# Questions?

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Space and Occupational Medicine Branch (SD3)  
NASA Johnson Space Center  
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